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# INTESTINAL INFECTIONS IN INFANTS

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In centuries far removed from the present, Greek writers [1] described gastro-intestinal disturbances or diseases accompanied by diarrhea to which adults and children were subject, especially at certain seasons of the year. Due emphasis was placed on the serious nature of these diseases, particularly among children. English and French physicians [2] of the eighteenth century observed the high mortality in young children brought about by such diseases, which they also recognized as having a seasonal incidence. Descriptive names that have long since become obsolete were applied by these men to the diseases; quaint theories were advanced to explain their cause, and heroic measures instituted to effect cures.

In 1777, in America, Benjamin Rush [3] recognized that there existed in towns along the Atlantic Coast a serious gastro-intestinal disease confined chiefly to children under 2 years of age. This disease, which was most prevalent in summer, had been unknown to the aborigines and to the early settlers, but seemed to have appeared when the population began to congregate in towns and villages. Certain aspects of this malady reminded him of Asiatic cholera which he had seen in Europe, hence he proposed for it the term "cholera infantum." "Cholera infantum" was used by him as a generic term to embrace the group of conditions which later were classed under the head of "summer

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1. Davison: Medicine **1**:391, 1922, quotes Hippocrates and Herodotus.

2. Cooke, J.: Plain Account of the Diseases Incident to Children, London, E. & C. Dilly, 1769, p. 11. Smith, H.: Letters to Married Women on Nursing and the Management of Children, first American edition, from the sixth London edition, Philadelphia, M. Carey, 1792, p. 6. Moss, W.: An Essay on the Management, Nursing and Diseases of Children from Birth, and on the Treatment and Diseases of Pregnant and Lying-In Women, Egham, England, C. Boult, 1794, p. 150. Leroy, A. V. L.: Médicine maternelle, Paris, Chez Mequignon L'Aine, 1803. Underwood, Michael: A Treatise on the Diseases of Children, London, J. Callow, 1811, p. 118.

diarrheas of infants." It had seldom been noted in Western Europe up to that time, probably, as suggested by Booker,[3] because little importance was attached to the lives of very young children.

However, as further inquiry was instituted into summer diarrheas of infancy, especially on this continent, it was thought that a uniform clinical picture was not presented by all cases. Some infants experienced a very mild temporary disturbance attributed to improper feeding; to this type the descriptive term "fermentative diarrhea" was applied. The presence of blood and pus in the intestinal excreta in other more severe cases led to the term "infectious diarrhea." "Cholera infantum," a term now obsolete, designated the most severe cases which showed marked dehydration and intoxication, and rapidly terminated fatally. Finkelstein,[4] in Germany, applied the term *alimentäre Intoxikation* (alimentary intoxication) to such cases, and his conception has been adapted on this continent as "acute intestinal intoxication."

The theories with regard to the cause or causes of such conditions are just as lacking in uniformity as are the descriptive terms. "Fermentative diarrhea" has been attributed to the action of bacteria present in the intestine on unsuitable food, mainly carbohydrate. Bacteriologic investigation of severe diarrheas in which blood and pus were manifested has revealed the presence of various species of dysentery bacilli, which organisms have then been considered the causative agent of "infectious diarrhea." Promulgated in Europe and adopted in America by some pediatricians and otolaryngologists [5] was the hypothesis that toxicity from masked infection of the mastoid region by hemolytic streptococci produced the gastro-intestinal symptoms in infants under 2 years of age which were diagnosed clinically as "acute intestinal intoxication."

In order to determine the validity of the various theories, an intensive investigation from both the clinical and the bacteriologic aspects was carried out in the Hospital for Sick Children,[6] Toronto, from October, 1928, to October, 1929, inclusive. This survey entailed the investigation of 172 cases, the symptoms of which led to a diagnosis of acute intestinal intoxication or were related to the symptoms suggested by that diagnosis. In order properly to evaluate the findings, 107 controls were subjected to similar investigation. The controls consisted of:

4. Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1924, vol. 4, p. 279.

5. Floyd, M. L.: Masked Mastoiditis Simulating "Alimentary Intoxication," Arch. Otolaryng. **1**:411 (April) 1925. Alden, A. M.: South. M. J. **19**:360, 1926. Alden, A. M., and Lyman, H. W.: Laryngoscope **35**:586, 1925. Marriott, W. McK.: Laryngoscope **35**:592, 1925. Lyman, H. W.: J. Missouri M. A. **22**:293, 1925. Jeans, P. C., and Floyd, M. L.: Upper Respiratory Infection as a Cause of Cholera Infantum, J. A. M. A. **87**:220 (July 24) 1926.

6. Brown, A., and others: South. M. J. **23**:107, 1930.

(*a*) 9 infants with mastoiditis; (*b*) 9 with pneumonia; (*c*) 2 with pyelitis; (*d*) 62 in the medical and surgical wards with symptoms in no way related to those with acute intestinal intoxication; (*e*) 8 in the outpatient department with symptoms in no way related to those of acute intestinal intoxication, and (*f*) 17 normal infants.

The clinical observations in regard to the condition of the middle ear and mastoid have been reported by Wishart,[7] who made the oto-laryngologic examinations and obtained the ear, nose and throat cultures, which were the only ones investigated bacteriologically. In consequence, cultures were not obtained from the upper respiratory tract of all 172 infants.

## DESCRIPTION OF CASES

*Social Class.*—The patients were entirely drawn from Greater Toronto, a city of approximately 750,000 population.

TABLE 1.—*Clinical Diagnosis on Admission According to Age and Seasonal Distribution of Cases*

| Diagnosis on Admission | Age in Months | | | | | Seasonal Distribution | |
|---|---|---|---|---|---|---|---|
| | 0-3 | 4-6 | 7-12 | 13-20 | Totals | Oct., 1928 to July, 1929 | Aug., Sept., Oct., 1929 |
| Acute intestinal intoxication | 24 | 27 | 35 | 7 | 93 | 15 | 78 |
| Dysentery | 0 | 0 | 1 | 0 | 1 | 1 | 0 |
| Fermentative diarrhea | 2 | 2 | 4 | 0 | 8 | 2 | 6 |
| Intestinal intoxication and fermentative diarrhea | 3 | 5 | 8 | 1 | 17 | 15 | 2 |
| Infectious intoxication | 10 | 12 | 9 | 2 | 33 | 6 | 27 |
| Miscellaneous | 4 | 6 | 6 | 4 | 20 | 9 | 11 |
| Totals | 43 | 52 | 63 | 14 | 172 | 48 | 124 |

Although all the patients entering the hospital with symptoms in any way suggestive of acute intoxication or diarrhea were submitted for investigation, it is significant that of the 172, 170 were in the public wards, only 2 being private patients. These patients came largely from the poorer district of the city lying close to the business center (as shown in the spot map, chart 1) where the people belong mostly to the laboring class, subject to the vagaries of industrial requirements, living under congested conditions, often in houses with poor sanitary conveniences.

*Seasonal Distribution.*—The monthly distribution of the cases is shown in chart 2. While patients were admitted throughout the year, a marked epidemic characteristic is shown in the sharp increase in August, September and October, in which months about 80 per cent of the cases occurred.

*Age and Sex Distribution.*—The youngest patient was aged 1 month, the oldest 20 months. The age distribution is shown in table 1. The

7. Wishart, D. E. S.: Relation of Infection of the Ear and Infection of Intestinal Tract in Infants, J. A. M. A. **95**:1084 (Oct. 11) 1930.

great preponderance in the first year, 158 of 172, is striking and suggests that the condition occurs either more frequently or with much greater severity in this group. The third three month period of life showed the greatest number of cases. It is possible that this distribution does not represent the general distribution but rather the more severe grades that required hospital care.

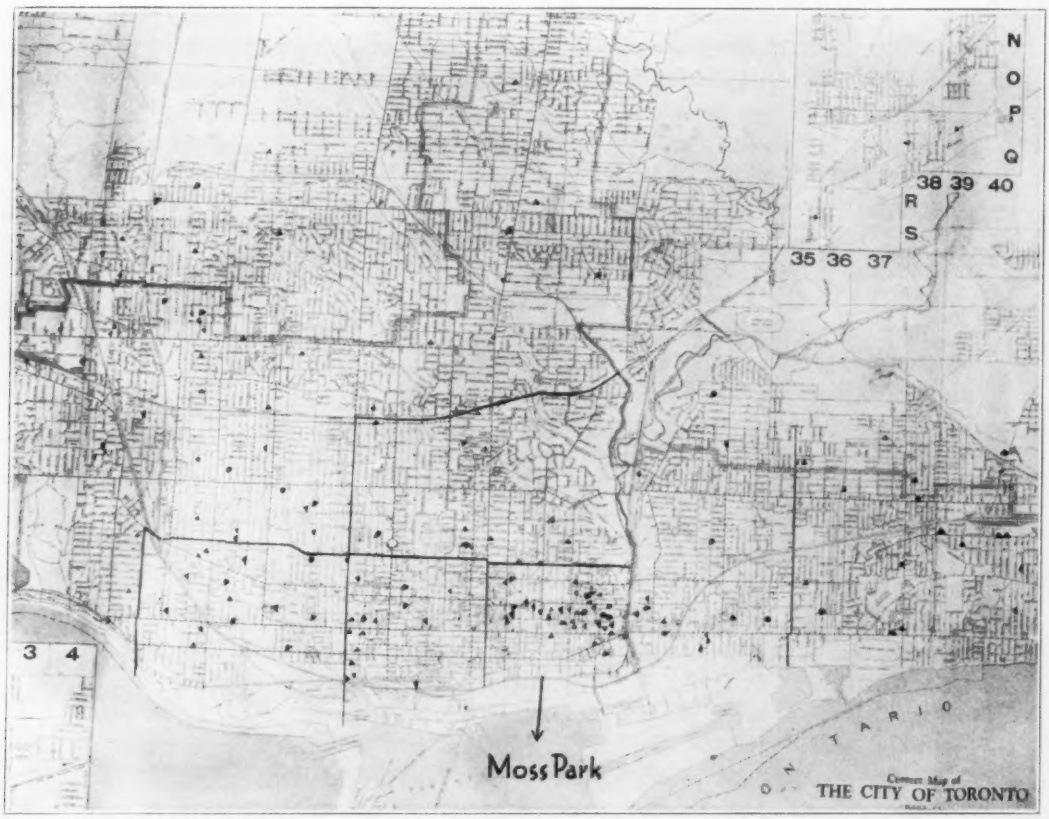


Chart 1.—Spot map showing location of cases of summer diarrhea, October, 1928-October, 1929.

Ninety-seven, or 57 per cent, of the patients were males; 75, or 43 per cent, were females. Deaths in males numbered 44; in females, 33. The incidence, mortality and case fatality rates according to age groups are shown in table 2.

*Clinical Diagnosis on Admission.*—Table 1 also indicates that the intoxication concept was general in this series of diagnoses. "Intoxication" in some form appeared in 143 of the 172 infants admitted with a clinical diagnosis. In 17 of these it was coupled with fermentative

diarrhea. Fermentative diarrhea alone was recorded only eight times and dysentery once.

An analysis of the seasonal incidence with reference to the clinical diagnoses on admission did not reveal any correlation. No one diagnosis predominated at any particular season.

*Clinical Symptoms Manifested by the Patients.*—The three cardinal symptoms of the clinical condition diagnosed as "acute intestinal intoxi-

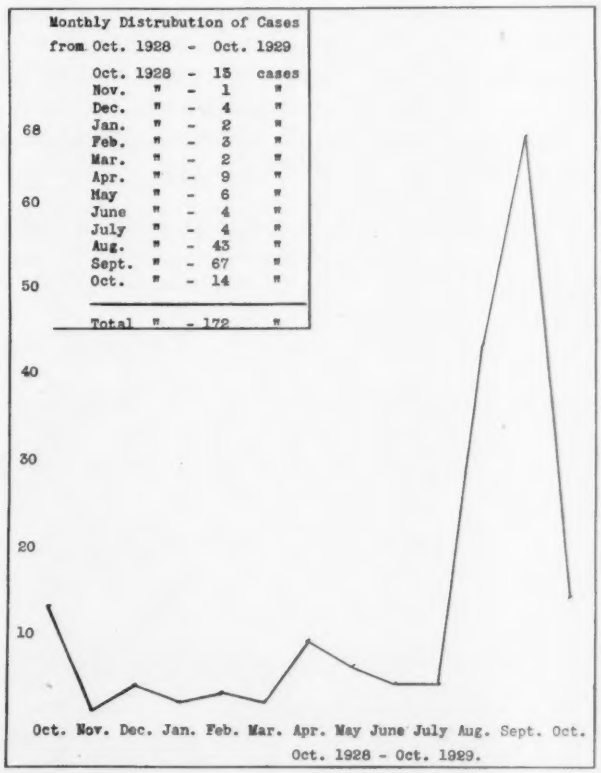
Monthly Distrubution of Cases
from Oct. 1928 - Oct. 1929
Oct. 1928 - 15 cases
Nov. " - 1 "
Dec. " - 4 "
Jan. " - 2 "
Feb. " - 3 "
Mar. " - 2 "
Apr. " - 9 "
May " - 6 "
June " - 4 "
July " - 4 "
Aug. " - 43 "
Sept. " - 67 "
Oct. " - 14 "
Total " - 172 "
68
60
50
40
30
20
10
Oct. Nov. Dec. Jan. Feb. Mar. Apr. May June July Aug. Sept. Oct.
Oct. 1928 - Oct. 1929.

Chart 2.—Graph showing the number of cases studied.

cation," namely, diarrhea, vomiting and drowsiness, characterized 106 cases. Diarrhea and vomiting were recorded in the histories of 146 cases. No vomiting was noted in 20 cases, and absence of diarrhea in 5. No data relative to vomiting and diarrhea were obtained in one case.

*Feeding History.*—It is of striking importance that only 7 of these infants were exclusively breast fed. Six were receiving supplementary feedings. A very high percentage, 79, were bottle fed. Eighteen, or about 11 per cent, were given soft diet suitable to their age.

*Duration of Illness and Mortality.*—An impression of an acute disease which commences suddenly, continues but a few hours or days, and terminates fatally, is acquired during the epidemic period, when within a short period of time there is a large influx of patients with severe cases, many of whom are practically moribund when admitted. That this conception is erroneous is shown by the fact that the history of only 1 of the 172 children showed a duration of illness as short as four days. Table 3 shows the duration of illness from onset of symptoms to death or recovery. Only 15 patients were ill seven days or less, and 42 had a clinical history of fourteen days or less; 130, or 61 per cent, of the patients were ill more than two weeks. All patients ill one week or less died; 34 of the 42 ill two weeks or less died. Therefore, 43, or 61 per cent, of all deaths occurred in the 130 cases with the longer duration of clinical symptoms.

TABLE 2.—*Incidence, Mortality and Fatality Rate According to Age Groups*

| Age Groups | Patients | Deaths | Fatality Rate |
|---|---|---|---|
| 0 to 6 months | 95 | 44 | 46.3 |
| 7 to 12 months | 63 | 26 | 41.3 |
| Over 12 months | 14 | 7 | 50.0 |
| | 172 | 77 | 44.8 |

TABLE 3.—*Total Duration of Illness from Onset*

| | Days | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Totals | 4 | 5 | 6 | 7 | 8-14 | 15-21 | 22-28 | Over 28 |
| Patients | 172 | 1 | 2 | 6 | 6 | 27 | 26 | 29 | 75 |
| Deaths | 77 | 1 | 2 | 6 | 6 | 19 | 15 | 13 | 15 |

## EAR, NOSE AND THROAT EXAMINATIONS

*Clinical.*—On admission to the hospital, 126 infants had no demonstrable aural involvement; 45 had definite otitis media, and in 1 the condition was "doubtful." Of the 126 infants who had normal ears on admission, otitis media developed in 65, or 51.5 per cent, thus making a total of 110 cases of otitis media, or 64 per cent.

Of the 82 controls who were admitted to the hospital, 53, or 63 per cent, had otitis media either on admission or during hospitalization. No cultures or examinations were made of the infants not hospitalized.

*Bacteriologic.*—Cultures from the ear were taken through a sterile speculum inserted after the external canal was thoroughly washed with alcohol. The cultures from the nasopharynx were obtained by swab through a sterile metal cannula inserted in the nostril. Cultures from the throat were obtained in the ordinary manner. All these were planted on Löffler's serum agar slopes and blood agar plates (10 per

cent human, very occasionally sheep's blood). Cultures were incubated for twenty-four hours after which colonies were selected for further identification.

The results of the bacteriologic examination of the ear, nose and throat in regard to the presence of hemolytic streptococcus are shown in table 4 (only cultures from the ear obtained when paracentesis was performed by D. E. S. Wishart were studied, 31 cases). It was considered expedient to exclude all other cultures from the ear from the investigation. In the same table are shown the results in the control group. It will be noticed that hemolytic streptococci were obtained from the patients with comparative rarity, less frequently, indeed, than from the controls. The finding of hemolytic streptococci in as many controls as is shown is evidence that these micro-organisms were not missed in selection. The various species of micro-organisms which

TABLE 4.—*Isolations of Streptococci from Upper Respiratory Tract of Patients and Controls*

| | Ear | | | | Nasopharynx | | | | Throat | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Patients Examined | Streptococcus | Streptococcus Hemolyticus | Per Cent Positive for Streptococcus Hemolyticus | Patients Examined | Streptococcus | Streptococcus Hemolyticus | Per Cent Positive for Streptococcus Hemolyticus | Patients Examined | Streptococcus | Streptococcus Hemolyticus | Per Cent Positive for Streptococcus Hemolyticus |
| Patients | 31 | 17 | 6 | 19 | 128 | 50 | 5 | 4 | 151 | 91 | 18 | 12 |
| Controls | | | | | | | | | | | | |
| A. Mastoiditis | 4 | 4 | 3 | .. | 0 | 0 | 0 | .. | 9 | 7 | 0 | .. |
| B. Miscellaneous controls | 19 | 8 | 6 | .. | 43 | 21 | 3 | .. | 71 | 58 | 14 | .. |
| Totals | 23 | 12 | 9 | 39 | 43 | 21 | 3 | 7 | 80 | 65 | 14 | 18 |

were identified are shown in table 5. The presence of Corynebacterium diphtheriae in one culture from the ear, in three from the nasopharynx and in one from the throat, and of meningococcus in one culture from the nasopharynx is of interest. A strain of B. dysenteriae Flexner was cultivated from one culture from the nasopharynx; it was also obtained from that patient's stool.

### STOOL EXAMINATIONS

*Patients.*—Cultures from the stool were obtained as soon as possible after the infants were admitted to the hospital. In order to avoid loss of significant micro-organisms by the use of old specimens, fresh stools were cultivated in every case. These were often induced by rectal swab. Mucus, pus or bloody shreds, when present, were transferred immediately to culture mediums. Any possible deleterious influence of saline, glycerin, etc., was thus entirely eliminated. The technic used for culture and identification of the organisms is indicated as a footnote to table 6 which shows the biologic reactions of the species identified.

Micro-organisms of definitely recognized pathogenicity were isolated in 27 cases, as shown in table 7, and species of possible significance, excluding B. morgani and B. paracoli, were isolated in 43 cases; 42 of the 172 cases investigated failed to yield any suggestive micro-organism. The isolation of B. dysenteriae Sonne in 13 cases is striking in view of the fact that no previous isolations had been reported in Canada.[8]

B. paratyphosus B was isolated in 9 cases, B. dysenteriae Flexner in 3 and B. dysenteriae Hiss-Russell and B. paratyphosus C in a case each. The species of less well established pathogenicity, such as B. dysenteriae Schmitz, B. paracoli, B. morgani, B. asiaticus, Fothergill's

TABLE 5.—*Bacterial Flora Cultures from the Upper Respiratory Tract of Patients and Controls*

| | Patients | | | Controls | | |
|---|---|---|---|---|---|---|
| | Ear | Naso-pharynx | Throat | Ear | Naso-pharynx | Throat |
| Number of examinations | 31 | 128 | 151 | 23 | 43 | 80 |
| Streptococcus hemolyticus | 6 | 5 | 18 | 9 | 3 | 4 |
| Other streptococci | 11 | 50 | 83 | 3 | 8 | 51 |
| Staphylococcus aureus | 4 | 20 | 29 | 8 | 6 | 19 |
| Staphylococcus albus | 18 | 33 | 44 | 13 | 14 | 37 |
| Staphylococcus citreus | 1 | 10 | 1 | 1 | 1 | 2 |
| Staphylococcus species | 1 | 6 | 8 | 1 | 1 | 0 |
| M. pharyngis-siccus | 2 | 27 | 55 | 2 | 9 | 30 |
| M. catarrhalis | 6 | 38 | 27 | 2 | 16 | 12 |
| Unclassified gram-negative cocci | 0 | 11 | 16 | 0 | 4* | 4 |
| Proteolytic bacilli | 3 | 3 | 0 | 0 | 0 | 0 |
| Colon group | 6 | 20 | 35 | 2 | 5 | 9 |
| B. paracoli | 0 | 1 | 0 | 0 | 0 | 1† |
| Dysentery bacilli | 0 | 2 | 0 | 0 | 0 | 0 |
| Unclassified gram-negative bacilli | 0 | 2 | 0 | 0 | 2 | 2‡ |
| Yeast | 1 | 4 | 15 | 0 | 0 | 7 |
| C. diphtheriae | 0 | 1 | 1 | 1 | 2 | 0 |
| C. xerosis | 3 | 7 | 6 | 4 | 1 | 4 |
| C. hofmanni | 0 | 4 | 1 | 0 | 0 | 0 |
| Negative | 2 | 2 | 2 | 0 | 3 | 1 |

* One culture was identified as M. meningitidis.
† This culture was hemolytic.
‡ One culture was a hemolytic strain of B. morgani.

bacillus, were isolated as the table shows more frequently. The significance of this will be discussed later. Table 7 shows the varieties of species isolated in individual cases. The finding of mixtures of species in a single case is probably accounted for by the fact that from ten to forty colonies were picked from the original plate and carried on to complete identification. In addition, several specimens from one case were frequently examined.

*Controls.*—The cultures from the stools of 107 controls yielded the results shown in table 8. Only one known pathogen, a strain of B. dysenteriae Flexner, was isolated; this control, however, gave a history of previous vomiting and diarrhea which probably explains the presence of the micro-organism. Table 9 shows the comparison of the

8. Johnston, M. M., and Brown, A.: Canad. Pub. Health J. **22**:445, 1931.

percentage frequency of the isolations of the species of questionable pathogenicity in the patients and controls. Much greater frequency of isolation from the cases of Schmitz' bacillus, Fothergill's bacillus, B.

TABLE 6.—*Biologic Reactions of the Various Bacterial Species* *

| | Number of Strains | Motile | Gas | Lactose | Dextrose | Maltose | Saccharose | Xylose | Mannite | Arabinose | Indol | Gelatin | Lead Acetate | Litmus Milk |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| B. dysenteriae Sonne | 13 | — | — | + Late | + | + | + or — | — | + | + | — | — | — | Acid Coagulated |
| B. dysenteriae Flexner | 4 | — | — | — | + | + or — | — | — | + | + or — | + or — | — | — | Alkaline |
| B. dysenteriae Schmitz (M. Research Council, A System of Bacteriology, London, His Majesty's Stat. Off., 1929, vol. 4, p. 216 | 18 | — | — | — | + | — | + or — | — | — | — | + or — | — | — | Alkaline |
| B. dispar (?)[a] | 5 | — | — | + Late | + | — | — | + | — | + | — | — | — | Acid Coagulated |
| B. morgani | 57 | + or — | + | — | + | — | — | — | — | — | + | — | + or — | Alkaline |
| B. paracoli | 34 | — | + | — | + | + | — | + | + | + | + | — | — | Alkaline |
| Fothergill's bacillus (Fothergill: J. Infect. Dis. 45 : 393, 1929 | 11 | — | + | + or — | + | + | + | + | + | + | + | — | — | Acid Coagulated |
| B. paratyphosus aertrycke | 9 | + | + | — | + | + | — | + | + | + | — | — | + | Alkaline |
| B. paratyphosus C | 1 | + | + | — | + | + | — | + | + | + | — | — | + | Alkaline |
| Proteus asiaticus | 9 | — | + | — | + | + | + | + | + | + | + | — | — | Alkaline |
| Proteus vulgarus | 16 | + | — | — | + | + | + | + | — | — | — | + | + | Alkaline Peptonized |
| B. paradiffluens (Castellani and Chalmers: Manuel of Tropical Medicine, ed. 3, London, Baillière, Tindall & Cox, 1919, p. 950) | 20 | + | — | — | + | — | + | + | — | — | — | + | + | Alkaline Peptonized |
| B. alkaligenes-fecalis | 16 | + | — | — | — | — | — | — | — | — | — | — | + | Alkaline |

* B. pyocyaneus was isolated in 6 cases; other proteolytic bacilli in 6 cases. B. morgani utilized galactose and levulose, and B. paratyphosus Beta utilized inosite and produced an acid reaction in Jordan's tartrate medium (Jordan and Harmon: J. Infect. Dis. 42 : 238, 1929). B. paracoli and B. paratyphosus C failed to utilize inosite.

The cultures of the feces were spread after incubation at 37 C. for an hour or so on eosin-methylene blue lactose agar, bromthymol blue lactose agar and MacConkey bile salt lactose agar plates. A total of 6 plates was regularly used primarily for each case. The bromthymol blue medium was found to be unsuitable, since it permitted a proteolytic "spreader" to grow across the plate, thus obscuring all other colonies, although in the absence of a "spreader" the differentiation of the lactose-utilizing and nonlactose-utilizing colonies was found to be quite satisfactory. Both other mediums restricted the "spreader" to individual colonies.

Suggestive single colony cultures were transferred from the differential plates to plain nutrient agar slopes, and identification of these cultures was then continued. Various carbohydrate and biologic reactions were then tested as shown in this table. The carbohydrates listed were regularly employed; where further differentiation was required additional carbohydrates were used. The indol tests were carried out after forty-eight hours' incubation in Dunham's peptone water medium, the Ehrlich method being used.

For further identification, agglutination tests were performed, the agglutinating serum produced in rabbits by known strains of the bacilli under consideration being used.

asiaticus and B. morgani at least suggests some causal relationship of these micro-organisms. The agreement in so far as B. paracoli and the proteolytic bacilli are concerned minimizes their importance from the standpoint of pathogenicity.

No micro-organisms of any apparent significance were isolated in 48 blood cultures. Similarly, cultures isolated from the urine were of no importance from the etiologic point of view.

### SEROLOGIC EXAMINATIONS

*Patients.*—Blood in many cases was tested for agglutinins with the various species of micro-organisms isolated from the stools. The results are shown in table 10. Agglutinins for B. dysenteriae Sonne [9] were found in 33 serums, for B. dysenteriae Flexner in 1, for B. paratyphosus B in 3, for B. morgani in 2, and for Fothergill's bacillus in 2. As the table shows, in certain cases agglutinins were found in the serums for species of bacteria that were not recovered from the stools

TABLE 7.—*Frequency of Association of Species Isolated from Stools of Patients*

| Species | Number of Strains | Frequency of Association of Species in Column 1 with: Alone | Sonne | Flexner | Schmitz | Dispar (?) | Para B | Asiaticus | Morgani | Paracoli | Fothergill | Proteolytic | Other Combinations |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Sonne | 13 | 6 | .. | .. | 1 | .. | .. | .. | 2 | .. | .. | 2 | 2 |
| Hiss-Russell | 1 | 1 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Flexner | 3 | 2 | .. | .. | .. | .. | .. | .. | .. | 1 | .. | .. | .. |
| Schmitz | 18 | 4 | 1 | .. | .. | .. | .. | .. | 2 | 1 | .. | .. | 10 |
| Dispar (?) | 5 | 1 | .. | .. | .. | .. | .. | .. | .. | .. | .. | 1 | 3 |
| Para B | 9 | 5 | .. | .. | .. | .. | .. | .. | .. | 1 | .. | 1 | 2 |
| Para C | 1 | 1 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Asiaticus | 8 | 3 | .. | .. | .. | .. | .. | .. | 1 | .. | .. | 1 | 3 |
| Morgani | 57 | 16 | 2 | .. | 2 | .. | .. | 1 | 0 | 1 | 5 | 11 | 19 |
| Paracoli | 34 | 14 | .. | 1 | 1 | .. | 1 | .. | 1 | .. | 1 | 6 | 9 |
| Fothergill | 11 | 1 | .. | .. | .. | .. | .. | .. | 5 | 1 | .. | 1 | 3 |
| Proteolytic | 44 | 11 | 2 | .. | .. | 1 | 1 | 1 | 10 | 5 | 1 | .. | 12 |

in those cases. This suggests that the micro-organism was being missed in culturing, a suggestion that later work substantiates.[8]

In certain instances no agglutinins were found in serums from cases in which pathogenic micro-organisms had been isolated from the stools. As far as this investigation is concerned, the blood may have been drawn before agglutinins were formed. In at least two instances blood taken immediately after the patient's admission to the hospital contained no agglutinins for the pathogenic species isolated from their stools

9. The details of satisfactory methods for carrying out agglutination tests for the Sonne dysentery bacilli have previously been reported (Johnston, M. M., and Brown, A.: Canad. Pub. Health J. **21**:395, 1930). With respect to the other bacilli, the requirements were less exacting. An eighteen hour agar slope culture was washed off with saline of $p_H$ 7.0, buffered with sodium and potassium phosphates. The suspension was diluted to an opacity about equivalent to a Macfarland no. 3 barium sulphate standard. After the serum dilutions were prepared and the suspension added, the tests were incubated in a water-bath at 56 C., usually for about eighteen hours. After this they were removed to the icebox for some hours before readings were made.

TABLE 8.—*Species of Gram-Negative Bacilli Isolated from Control Stools*

| | Mastoids | Pneumonias | Small Poorly Developed | Pyelitis | Miscellaneous Diagnoses | Child Welfare | Outpatient Dept. | Total |
|---|---|---|---|---|---|---|---|---|
| Number of cases | 9 | 9 | 6 | 2 | 56 | 17 | 8 | 107 |
| Negative | 7 | 6 | 3 | 0 | 31 | 6 | 4 | 57 |
| Species | | | | | | | | |
| Schmitz | .. | .. | .. | .. | .. | 1 | .. | 1 |
| Flexner | .. | .. | 1 | .. | .. | .. | .. | 1 |
| Dispar (?) | .. | .. | .. | .. | 2 | .. | .. | 2 |
| Asiaticus | .. | .. | 1 | .. | .. | .. | .. | 1 |
| Morgani | .. | 1 | .. | 1 | 5 | 6 | 1 | 14 |
| Paracoli | 2 | .. | 2 | .. | 9 | 2 | 3 | 18 |
| Paradiffluens | .. | .. | .. | 1 | 6 | 2 | .. | 9 |
| Proteus vulgaris | .. | .. | .. | 2 | 3 | .. | .. | 5 |
| Pyocyaneus | .. | 1 | 1 | 1 | 2 | .. | .. | 5 |
| Alkaligenes | .. | .. | .. | .. | .. | 1 | .. | 1 |
| Unidentified gram-negative bacillus | .. | 1 | .. | .. | 1 | 1 | .. | 3 |

TABLE 9.—*Percentage Frequency of Isolation of Species of Less Well Recognized Pathogenicity from Patients and Controls*

| | Schmitz' Bacillus | Fothergill's Bacillus | B. asiaticus | B. morgani | B. paracoli | Proteolytic Bacillus |
|---|---|---|---|---|---|---|
| Patients | 10 | 6 | 5 | 33 | 20 | 25 |
| Controls | 1 | 0 | 1 | 13 | 17 | 18 |

TABLE 10.—*Results of Agglutination Tests with Various Bacterial Species and Serums of Patients and Controls*

| Species | | Stool | Serum | Number Positive in Highest Serum Dilutions in Which Agglutination Occurred | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | No. | 20 | 40 | 80 | 160 | 320 | 640 | 1,280 | 2,560 |
| B. dysenteriae Sonne | Patients | Pos. | Pos. | 7 | .. | .. | 2 | 1 | 3 | 1 | .. | .. |
| | | Neg. | Pos. | 26 | .. | .. | 3 | 4 | 13 | .. | 5 | 1 |
| | | Pos. | Neg. | 2 | .. | .. | .. | .. | .. | .. | .. | .. |
| | | Neg. | Neg. | 57 | .. | .. | .. | .. | .. | .. | .. | .. |
| | Controls | Neg. | Pos. | 2 | 1 | 1 | .. | .. | .. | .. | .. | .. |
| | | Neg. | Neg. | 26 | .. | .. | .. | .. | .. | .. | .. | .. |
| B. dysenteriae Flexner | Patients | Pos. | Pos. | 1 | .. | .. | .. | 1 | .. | .. | .. | .. |
| | | Neg. | Neg. | 93 | .. | .. | .. | .. | .. | .. | .. | .. |
| | Controls | Neg. | Neg. | 19 | .. | .. | .. | .. | .. | .. | .. | .. |
| B. paratyphosus B | Patients | Pos. | Pos. | 2 | .. | .. | .. | 1 | .. | 1 | .. | .. |
| | | Neg. | Pos. | 1 | .. | .. | .. | 1 | .. | .. | .. | .. |
| | | Neg. | Neg. | 117 | .. | .. | .. | .. | .. | .. | .. | .. |
| | Controls | Neg. | Neg. | 28 | .. | .. | .. | .. | .. | .. | .. | .. |
| B. morgani | Patients | Pos. | Pos. | 2 | .. | .. | 1 | 1 | .. | .. | .. | .. |
| | | Pos. | Neg. | 38 | .. | .. | .. | .. | .. | .. | .. | .. |
| | | Neg. | Neg. | 11 | .. | .. | .. | .. | .. | .. | .. | .. |
| | Controls | Neg. | Neg. | 28 | .. | .. | .. | .. | .. | .. | .. | .. |
| Fothergill's bacillus | Patients | Pos. | Pos. | 2 | .. | .. | .. | 2 | .. | .. | .. | .. |
| | | Pos. | Neg. | 5 | .. | .. | .. | .. | .. | .. | .. | .. |
| | | Neg. | Neg. | 60 | .. | .. | .. | .. | .. | .. | .. | .. |
| | Controls | Neg. | Pos. | 3 | 2 | .. | .. | 1 | .. | .. | .. | .. |
| | | Neg. | Neg. | 9 | .. | .. | .. | .. | .. | .. | .. | .. |

while blood drawn seven days later agglutinated that species in dilutions of 1 : 320. Again the technic may have been at fault. A complete explanation of the results of the agglutination tests, however, awaits further work. Agglutination tests in these cases thus yielded more evidence of infection than did cultures from the stool. However, in a further series of 170 cases studied in 1930 and 1931, 113, or 67 per cent, showed positive stool cultures.[10] Additional experience with the Sonne bacillus since the 1928-1929 series was studied has materially assisted in producing these higher results.[11]

No serums were found to contain agglutinins for B. dysenteriae Schmitz, B. asiaticus, B. dispar (?), B. paratyphosus C or the proteolytic bacteria.

*Controls.*—Blood was obtained from 28 controls, 7 normal infants and 21 infants whose clinical symptoms could not lead to a diagnosis of acute intestinal intoxication. No agglutinins were demonstrated for B. paratyphosus B, B. dysenteriae Schmitz, B. dispar (?), B. dysenteriae Flexner and B. morgani. Two serums gave reactions in 1 : 20 and 1 : 40 dilutions, respectively, with B. dysenteriae Sonne. Three serums reacted with Fothergill's bacillus, 2 in dilutions of 1 : 40, 1 in a dilution of 1 : 160. No cultures were isolated in these cases.

The difference in the observations is striking and is convincing evidence of the significance of infection in the cases as contrasted with the control group.

### POSTMORTEM EXAMINATIONS

*Patients.*—Postmortem examination was performed in 19 cases.[12] In 11 there had been clinical evidence of otitis media, which diagnosis was corroborated by the postmortem examination. Nine of these cases showed bilateral infection; in 5 there was anatomic evidence of mastoiditis in addition. Nonhemolytic streptococci were isolated at autopsy in 10 of the 11 cases showing otitis media, and in 5 of 8 that did not show any other evidence of infection, clinically or anatomically. Hemolytic streptococcus was isolated from one middle ear, although there was no other evidence of involvement present. From the stool in 9

10. Johnston, M. M.; Brown, A., and Kaake, M. J.: Intestinal Infections in Infants and in Children—1930 and 1931 Series, Am. J. Dis. Child., to be published.

11. Johnston, M. M., and Kaake, M. J.: Canad. Pub. Health J. **23**:159 (April) 1932.

12. Unless great care was exercised, bacterial contamination of the mastoid antrums from outside sources could easily occur during the examination of the head, thereby invalidating the bacteriologic results. A method was devised which obviated that possibility satisfactorily. Dr. I. H. Erb, the hospital pathologist, removed the brain and then seared the bony structure over the antrum with a hot iron; a soldering iron was found to be a convenient instrument. An opening was made in the sterile area with a sterile awl. A sterile capillary pipet was inserted through the opening thus prepared and purulent material, if present, was then withdrawn. The culture material was immediately planted on blood agar plates which had been taken to the postmortem room.

of the 19 cases pathogenic micro-organisms had been isolated; in 3 others there was serologic evidence of infection with species of the colon-paratyphoid-dysentery group, and in another case serologic evidence of infection with Fothergill's bacillus. This indicates that the cases that came to autopsy were quite representative of the groups as a whole.

B. dysenteriae Sonne was isolated from the gallbladder in a case in which it had not been previously obtained from the stool culture. A strain of B. dysenteriae Flexner and one of B. dysenteriae Schmitz were cultivated from the colon in a case in which only B. dysenteriae Sonne had been found on stool culture. The latter bacillus was also isolated from the colon. The Schmitz bacillus was obtained from the colon and gallbladder in a case in which it had previously been cultured from the stool.

TABLE 11.—*Relation of Middle Ear Condition at Postmortem Examination to Organisms Found in Stool and by Agglutination in Patients and Controls*

| | Number | Without Otitis Media at Autopsy | With Otitis Media at Autopsy |
|---|---|---|---|
| Autopsies on patients | 19 | 8 | 11 |
| Streptococcus isolated | 15 | 5 | 10 |
| Streptococcus hemolyticus | 1 | 1 | 0 |
| Stool culture | 9 | 3<br>Sonne, 1<br>Sonne, Flexner and Schmitz, 1<br>Schmitz, 1 | 6<br>Sonne, 2<br>Sonne and Para B, 1<br>Fothergill's bacillus, 1<br>Asiaticus, 1<br>Morgani, 1 |
| Serum agglutinated | 4 | 2<br>Para B, 1:160, 1<br>Sonne, 1:1,280, 1 | 2<br>Sonne, 1:320, 1<br>Fothergill's bacillus, 1:160, 1 |
| Control | | | |
| Autopsies | 9 | 2 | 7 |
| Streptococcus isolated | 6 | 0 | 6 |
| Streptococcus hemolyticus | 5 | 0 | 5 |

*Controls.*—Postmortem examination was performed on 9 controls, in 7 of which there had been previous clinical evidence of otitis media. From 5 of the 7, hemolytic streptococcus was obtained as shown in table 11.

## CONTACT HISTORIES

Some data were collected concerning the incidence of diarrheas in other members of the families from which our cases were collected. In eleven families, eleven other persons had been ill a few days prior to the onset of the infant's complaint. In each of three families two children were ill at the same time; both children in two of the families and one of the children in the third were admitted to the ward at the same time. B. dysenteriae Sonne was isolated from the stool of one child, and serum of the second child agglutinated that species in a dilution of 1 : 160, although no culture was isolated from her stool. From one of the second pair of children, B. dysenteriae Sonne was isolated. No culture and no serum were obtained from the second child. The

mother of these children had suffered with diarrhea previous to the illness of her children. No suggestive cultures were isolated from one examination of stool from the members of the household other than the hospitalized patients. B. dysenteriae Sonne was isolated from the stool of an older sister of another patient whose stool culture contained B. dysenteriae Sonne. There was no history of diarrhea immediately prior to the baby's illness, and no data concerning a similar malady suffered by any member of the family could be elicited from the mother. However, she stated that her husband had served with the Canadian Expeditionary Force and was reported to have had dysentery during his service. His stool culture was negative when examined. The other thirty contact specimens from the remaining families were negative when examined.

The bottle used by the infant was retained and the contents cultured in seven cases without finding any species of dysentery or paratyphoid bacilli. The feedings were not sterile in any instance, but the B. coli and other bacterial species might have entered through the nipple opening.

Studies of flies were undertaken in order to see what species of bacteria, if any, were harbored and distributed by that agency. The flies were gathered in average homes in various quarters of the city. No specimens were taken from the homes of patients while the infants were in the hospital. However, they were collected while the epidemic was at its height from homes without any history of illness with intestinal manifestations. A strain of B. dysenteriae Flexner from one fly and two strains of B. dispar(?) from each of two other flies were obtained.

### NOMENCLATURE USED TO DESIGNATE THE CLINICAL SYMPTOMS

Approximately 54 per cent of the 172 infants were admitted to the hospital with their clinical symptoms diagnosed as "acute intestinal intoxication." In 8 cases the symptom complexes were designated "fermentative diarrhea." No evidence of the response on the part of the patient's serum in so far as agglutinin formation is concerned is implied by this clinical category. Hence, the presence of agglutinins in the serum of infants whose clinical symptoms were so diagnosed would not be anticipated.

Routine examinations for blood or pus in the stool were not carried out. Nevertheless, blood and pus were observed in the stools of 16 patients, 10 of whom were admitted with a clinical diagnosis of "acute intestinal intoxication." The stools of 3 of the 10 infants yielded dysentery bacilli, and that of the fourth, a paratyphoid strain. The serums of all of these patients agglutinated the homologous strain. In addition, the serums of 4 patients whose stools showed blood and pus and whose cultures were negative agglutinated pathogenic bacilli.

Table 12 shows the diagnosis in 7 cases in which the presence or absence of blood and pus in the stool had been noted and the results of the bacteriologic and serologic examinations.

From this table it is seen that the isolation of pathogenic micro-organisms was not confined to patients admitted with clinical diagnoses indicative of infection. No one species was isolated consistently from patients whose clinical symptoms led to only one clinical diagnosis on admission. The same species was cultivated from the stools of patients admitted under the various diagnoses of acute intestinal intoxication, fermentative diarrhea, etc. This is strong evidence, therefore, that the clinical diagnoses refer to one condition, namely, gastro-intestinal infection.

It might also be noted that the finding of blood and pus in the stool is not confined to dysentery caused by dysentery strains as it was observed in the stool in a case in which B. paratyphosus B was isolated.

TABLE 12.—*Diagnosis, Bacteriologic, Serologic and Stool Observations*

| Name | Diagnosis on Admission | Stool Characteristics | Bacteriologic Observations | Serologic Observations |
|---|---|---|---|---|
| Bch. | Fermentative diarrhea | Blood and pus | Negative | Sonne, 1:1,280 |
| McG. | Intestinal intoxication | Blood and pus | Negative | Sonne, 1:320 |
| McI. | Intestinal intoxication | Blood and pus | B. dysenteriae Flexner | Flexner, 1:160 |
| R. | Intestinal intoxication | Blood and pus | Fothergill's bacillus | Fothergill's 1:160 |
| S. | Dysentery | Blood and pus | B. paracoli | Paracoli, 1:640 |
| F. | Pneumonia; intestinal intoxication | Blood and pus | B. paratyphosus Aertrycke | Aertrycke, 1:320 |
| W. | Intestinal intoxication | Blood and pus | B. dysenteriae Sonne | Sonne, 1:80 |

## COMMENT

With reference to the hypothesis that masked mastoid infection may be the cause of acute intestinal intoxication, the following data gleaned from the study of the upper respiratory tract may be emphasized.

There was complete absence on admission of demonstrable ear complications in 126 children who had definitely established intestinal symptoms. In 62, or 36 per cent, of the total cases there was no evidence clinically, at any time, of involvement of the middle ear or mastoid. This, of course, does not rule out the possibility of masked mastoid infection. However, in the 110 patients who finally showed clinical evidence of otitis media, there is no suggestion that this involvement was an extension of a previous masked infection of the mastoid. The control group which showed as high a percentage of clinical otitis media did not manifest the symptoms of acute intestinal intoxication. Wishart's [7] analysis of the histories of infants on whom mastoid operations were performed showed that any of the symptoms of acute intestinal intoxication were seldom encountered. Moreover, the fact that otitis media is a frequent complication which accompanies the clinical

conditions in many cases in the infant ward without producing evidence of acute intestinal intoxication is strong evidence that the symptoms of acute intestinal intoxication are not related to involvement of the middle ear or mastoid.

Nor does the bacteriologic evidence offer any support of the masked mastoid infection theory. From only 6 of the 31 cases in which cultures from the ear were examined was Streptococcus haemolyticus cultivated, a finding altogether too infrequent to suggest etiologic relationship of that micro-organism to acute intestinal intoxication. Streptococcus haemolyticus was isolated six times in 19 miscellaneous controls and in 3 of 4 cases of mastoiditis, although there was no similarity whatever in the symptoms of these children and those manifested by the cases under consideration.

Postmortem examination in 19 cases demonstrated evidence of mastoid infection in only 5, and of otitis media in 11 cases. If mastoiditis or otitis media could be considered the cause of symptoms of acute intestinal intoxications, anatomic evidence of such a pathologic condition should be demonstrable in practically all the cases. The fact that 8, or 42 per cent, of cases examined, post mortem, showed no evidence of any involvement in the mastoid cells shows that this anticipated result was not realized and practically furnishes sufficient basis in itself to warrant discarding the hypothesis that middle ear or mastoid infection is the cause of acute intestinal intoxication. Support of this view is supplied by the fact that in 9 control cases definite anatomic evidence of middle ear involvement was found without those cases displaying the clinical symptoms of acute intestinal intoxication.

Streptococcus haemolyticus was isolated only once in the 19 cases in which autopsy was performed; in that case there was no suggestion anatomically of middle ear or mastoid infection. Hemolytic streptococci were cultivated in 5 of the 9 controls at postmortem examination. These observations lend no support to the contention that masked infection of the mastoid with hemolytic streptococcus is the cause of acute intestinal intoxication, nor have data evolved from this survey shown that such infection can ever produce the cardinal symptoms of acute intestinal intoxication.

The finding of definitely pathogenic micro-organisms belonging to the colon-typhoid-dysentery group in 27 of 172 cases, and of micro-organisms of less well recognized pathogenicity in 36 additional cases, with the serologic observations raising the definite evidence of infection to 27 more cases, or definite infection in 54, or 31 per cent, and probable infection in a total of 90, or 52 per cent, of the cases is by far the most significant finding in our investigation. Contrasted with the parallel finding that such evidence of infection was found only once in the controls (and was readily explicable in that case) the only tenable

conclusion from this investigation is that the clinical symptoms in these cases were due directly to gastro-intestinal infection. The isolation of bacterial species of less well established pathogenicity, such as the Schmitz bacillus, in 18, or 10 per cent, of the cases, and in but 1, or about 1 per cent, of the controls, strongly suggests that such species may be pathogenic.

The evidence of illness in contacts and the finding of similar micro-organisms in flies as were isolated from patients support the contention that gastro-intestinal infection is the cause of acute intestinal intoxication and suggests that its mode of spread is entirely similar to that of other better recognized infections.

## SUMMARY

To test the validity of the various hypotheses as to the cause of acute intestinal intoxication, 172 patients with acute intestinal intoxication or related diagnoses and 107 controls were subjected to clinical investigation as well as bacteriologic survey of the flora of the upper respiratory tract and gastro-intestinal tract. Although evidence of late involvement of the middle ear developed in 63 per cent of the cases, there was similar involvement in over 60 per cent of the controls who showed no evidence of acute intestinal intoxication. Hemolytic streptococci were isolated very rarely from the ear, nose and throat in the patients either during life or post mortem. Hemolytic streptococci were isolated more frequently from controls both during life and post mortem, although these showed no symptoms suggestive of acute intestinal intoxication.

Evidence was found bacteriologically or serologically of infection with pathogenic micro-organisms of the colon-paratyphoid-dysentery group.

## CONCLUSION

Acute intestinal intoxication is not caused by masked mastoid infection.

Acute intestinal intoxication, fermentative diarrhea, infectious diarrea, dysentery and summer diarrhea are synonyms indicating one condition—a gastro-intestinal infection with species of the colon-paratyphoid-dysentery group of bacilli.

# RAW APPLE DIET IN THE TREATMENT OF DIARRHEAL CONDITIONS IN CHILDREN

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The efficacy of a diet of raw apples in the treatment of diarrheal conditions in children has long been known in many parts of Germany by the populace. Occasionally brief mention of the value of raw apple has been made by medical authorities. It was first used systematically in the Kindersanatorium at Koenigfield by Sister Frieda Klimsch. Within the last three years this form of therapy has been advocated a great deal in Germany by the physicians, and several articles have appeared in the literature. All have reported favorable results.

Moro [1] described an apple diet which he used successfully in the treatment of fifty-two patients suffering from various diarrheal conditions. His patients ranged from 3 months to 10 years of age. He recommended from 500 to 1,500 Gm. of grated raw ripe apple daily for two days, depending on the age of the child. This corresponds to about seven to twenty medium-sized apples, and is sufficient to cover the water and nutritional requirements for that period. Wolff [2] obtained favorable results in one hundred and fifty cases. He found that it was occasionally necessary to continue the diet for four days instead of the usual two days. If the diet is properly individualized, the results are completely satisfactory. Other clinicians who have successfully used this form of therapy are Melentieva,[3] Heisler [4] and Kollmann.[5]

A review of the literature reveals only the few articles cited on the raw apple in the treatment of diarrheal conditions in children. Therefore it seemed that a report of the method and the results that I observed should prove valuable in serving to acquaint the physician better with a new and highly satisfactory form of treatment of diarrhea in children.

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Presented before the Milwaukee Pediatric Society, Oct. 14, 1931.

1. Moro, E.: Zwei Tage Apfeldiät (roh und gerieben) zur Behandlung diarrhöischer Zustände im Kindesalter, Klin. Wchnschr. **8**:2414 (Dec. 24) 1929.

2. Wolff, S.: Die Morosche Apfeldiät zur Behandlung diarrhöischer Zustände, Deutsche med. Wchnschr. **56**:2211 (Dec. 26) 1930.

3. Melentieva, E. P.: Raw Apples in the Treatment of Diarrhea in Children, Pediatrya **14**:424 (Oct.) 1930.

4. Heisler, A.: Rohe-Apfel-Tage, ein neues Verfahren zur Behandlung diarrhöischer Zuztände, Med. Welt **4**:1394 (Sept. 27) 1930.

5. Kollmann, A.: Apfelkost bei Durchfallsstörungen im Saüglings- und Kleinkindesalter, Med. Welt **4**:1067 (July 26) 1930.

The treatment consists of a diet of only scraped raw apple. Completely ripe and mellow fruit should be used. After the fruit has been peeled and cored, it is scraped to a pulp with a knife or rubbed on a grater. The child receives from 1 to 4 tablespoonfuls or more of this pulp every hour or two for forty-eight hours. The amount given varies with the age of the patient. The average number of tablespoonfuls of apple administered per day for the two days on the diet was approximately 30 in the cases here reported. Sometimes sugar was added to the fruit because a child objected to the sour taste. Nothing should be given besides the apple unless the patient craves liquids or is toxic. In those conditions weak black tea is allowed in small amounts. It is possible to add banana pulp to the apple and obtain favorable results if the apple alone is refused. This makes the apple more palatable in many cases.

After forty-eight hours on this therapy the patient is given a transitional diet containing no milk or vegetable as follows:

7:30 a. m.
Cooked cereal (without milk)
Toast
Cocoa, 1 cupful (made of water)

12:00 noon
Soup with rice
Potato gruel
Scraped beef
Toast

3:00 p. m.
Toast and tea

6:00 p. m.
Cereal (without milk) or cottage cheese
Toast
Banana
Cocoa (made of water)

The child is kept on this diet for forty-eight hours, and then gradually returned to his normal diet. Milk is the next item added, then vegetables, and the fruits last.

Treatment should be instituted as soon as possible after the onset of symptoms. However, after an analysis of my cases I concluded that there is apparently no relation between the results obtained and the time of beginning treatment. The raw apple therapy was started in from eight hours to two months after the appearance of the diarrhea in this series of cases.

I have used this treatment for diarrhea for over a year in a total of seventy cases. The majority, or fifty of the patients, were cared for in the home or at the office; the remaining patients were hospitalized

and hence were under more careful observation. Patients seen once or twice only are not included in this series.

The ages ranged from 9 months to 11½ years. Three were under 1 year of age, twenty-three were between 1 and 2 years, twenty-seven were between 2 and 5, nine were between 5 and 7 and eight between 7 and 12.

The types of diarrhea observed may be given as follows: Thirty-eight patients had enteritis, twenty had parenteral dyspepsia, seven had dyspepsia of dietetic origin and five had subacute colitis. Six of the seventy patients had definite evidence of toxicosis; five were from the enteritis group and one from the parenteral dyspepsia group.

The predominating symptoms noted in these patients were fever, frequent loose stools, abdominal pain, toxicosis and convulsions. The effect of an apple diet on these is here described.

## FEVER

All the patients with enteritis had an elevation of temperature at the time the treatment was started. The highest temperature was 106 F., while the lowest was 100 F. (rectal). The usual or average was 102 F. (rectal). In thirty-three patients the temperature was normal within ninety-six hours after the onset of treatment. The average case showed a normal temperature in forty-eight hours. The earliest normal temperature occurred twelve hours after treatment was instituted.

Fifteen of the patients with parenteral dyspepsia had an elevation of temperature over 100 F. just previous to starting the treatment. Five had a temperature of less than 99.5 F. The highest temperature was 104 F., while the usual average was from 101 to 102 F. In these fifteen children showing an elevated temperature when treatment was started, the temperature reached normal at the latest in ninety-six hours. The earliest normal temperature occurred thirty hours after treatment was begun. The average period was seventy-two hours. In the five patients having a normal temperature or less than 99 F., there was no increase in temperature after starting treatment.

The highest temperature in the seven cases of dietetic dyspepsia was 101 F. The usual or average was from 99 to 99.5 F. Three patients had normal temperatures. In the four patients with fever, the temperature became normal within thirty-six hours.

In the five cases of subacute colitis the temperatures were 101, 99.6, 100, 99.4 and 99.8 F. In four cases the temperatures were normal in twenty-four hours. In the other the elevation of temperature persisted for a short time owing to coryza and nasopharyngitis. Five patients who broke treatment or failed to follow orders are not included. However, in none of these did the temperature become higher after the treatment was started than it was just prior to beginning the diet.

STOOLS

The character of the stools deserves considerable attention. In thirty-eight cases of enteritis the average number of stools for the twenty-four hour or part of the twenty-four hour period before treatment was started was twelve, the greatest number of stools in twenty-four hours in any one case being thirty-two, while the least number was four. For thirty-seven cases the average number for the first twenty-four hours on the diet was four, the greatest number was twenty-two and the least none. For the second twenty-four hour period on the apple diet the average number of stools was three, the greatest number was fifteen and the least was none.

In the seven cases of dietetic dyspepsia the average number of stools for twenty-four hours, preceding treatment, was seven, the maximum was ten and the minimum five. For the first twenty-four hours after starting the regimen the average number of stools was one, the greatest number four and the least none. The average number for the second twenty-four hour period was two.

In the five cases of colitis (subacute) the average number of stools for the twenty-four hours preceding treatment was seven, the maximum was eight and the minimum five. The first twenty-four hours after treatment was started the greatest number was six, the least three and the average four. The second twenty-four hours after treatment was started the greatest number of stools was four, the least none and the average one.

FORMED STOOLS

Frequent loose stools are the cardinal symptom in these cases, so the consideration of the time of appearance of formed stools is interesting. On the average, formed stools appeared in twenty-four hours or less in all the cases. In thirty-six of thirty-eight cases of enteritis in which the diet was followed at least one day the results were as follows: The average time elapsing between the beginning of treatment and the appearance of formed stools was twenty-three hours. The longest time for the formation of stools was forty-eight hours, and the shortest, three hours and forty-five minutes.

In the nineteen cases of parenteral dyspepsia (one patient having broken treatment in the first twenty-four hour period) the average time of appearance of formed stools was in twenty-four hours. The latest appearance of formed stools was in thirty-six hours, and the earliest, in twelve hours.

In the seven cases of dietetic origin the average time of appearance of formed stools was nineteen hours, the earliest twelve hours and the latest thirty hours.

In the five cases of subacute colitis the stools were formed within twenty-four hours.

### MUCUS

Mucus was present in the stools in all the cases of enteritis, in sixteen of the twenty cases of parenteral dyspepsia, in five of the seven cases of dietetic dyspepsia and, in the five cases of colitis. In thirty-three of the cases of enteritis in which there was no interruption of treatment, the average time for the disappearance of mucus was sixty-one hours, the earliest twenty-four hours and the latest six days.

In the sixteen cases of parenteral dyspepsia showing mucus and following the diet for twenty-four hours, mucus disappeared from the stools, on an average, forty-three hours later.

In the five cases of dietetic dyspepsia showing mucus, there was no mucus after about thirty-two hours. In the five cases of colitis, mucus disappeared from the stools in about fifty-nine hours.

In the cases of enteritis the average time of disappearance of blood and pus was in thirty-four hours (except for occasional traces). Blood and pus usually disappeared from the stool before the mucus.

### PAIN

Abdominal pain was almost a constant symptom in the older children who could interpret their sensations accurately. From observation it was apparently present in all of the cases in a greater or less degree. In the older children, on whose statements one could rely, pain was not increased by the diet and usually disappeared rapidly. Two patients had severe abdominal pain and cramps in the limbs, which rapidly disappeared on treatment with scraped raw apple. This prompt action on abdominal pain is mentioned by other observers.

### TOXICOSIS

Toxicosis was present in six children. Five of the cases of enteritis showed evidence of toxicosis before the institution of the treatment. One of these patients was in a state of acidosis, and the treatment was stopped because she was unable to retain apple. In the cases showing toxicosis alone the raw apple was continued, and the toxic symptoms disappeared in all cases in thirty-six hours. One of the cases of parenteral dyspepsia showed evidence of toxicosis. In this patient the toxic symptoms disappeared within twenty-four hours after starting treatment.

Three of the patients with enteritis had convulsions just prior to the beginning of treatment. None of them had any more convulsions during the dietetic regimen.

Relapses rarely occurred in any of the cases studied.

Various theories have been advanced regarding the efficacy of this treatment. Moro [1] thinks that it is due to the fact that the apple pulp

provides a filling that is not irritative and that tranquilizes the motor apparatus of the intestine. The pulpy mass passing through the intestine not only effects a mechanical purification, but acts as an absorbent. Moro expressed the belief that it is to the tannin-containing principle of the apple that much of the success can be attributed. He contended that the tannic acid by virtue of its astringent property forms a protective membrane over the surface so that, after a fashion, the cells are protected against chemical, bacterial and mechanical injury, and therefore against all inflammatory irritation.

Winckel [6] also attributes the beneficial effect of the apple diet to the tannic acid.

Heisler [7] feels, on the contrary, that the malic acid in the apple is primarily responsible for the beneficial effects. Next in importance is the mechanical cleansing effect of the grated apple and, lastly, the tannin. In this respect he is supported by the fact that the fruit juices, like lemon juice, produce similar results.

Kohlbrugge [8] maintained that just as good results can be obtained by the use of lemon juice, and that the good effect following the apple diet is due to the fruity acid present. He therefore also suggested the giving of unpeeled, finely grated apple, since the peel and the layer just below it are richer in acid than is the pulp. He does not think that tannin plays an important rôle, since many diarrheal conditions are not benefited by the addition of tannin medication (e. g., a proprietary form of albumin tannate) to the customary diet of rice, arrowroot, etc.

Malyoth,[9] in a lengthy treatise on the subject, expressed the belief that the efficacy of the apple diet is attributable to a substance known as pectin. This substance is present in the juice of many fruits, including apples, and by virtue of its colloidal and its inherent buffer property it has the ability of regulating the hydrogen ion concentration. Also because of its colloidal nature, it has the power of absorbing both endogenous and exogenous poisons. Because of its calcium and magnesium content it acts as an inhibitor of peristalsis. As grated apple contains finely divided cellulose combined with pectin, a favorable medium is provided for the bacteria present in the intestine. These bacteria are then absorbed and encompassed by this mixture like a sponge; they are then excreted. Likewise, the amines which originate in the dysfunction of the intestine are absorbed and carried away.

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6. Winckel, M.: Apfeldiät und die Rolle des Gerbstoffs, Med. Welt **4**:1068 (July 26) 1930.

7. Heisler, A.: Rohe Apfel-Diät bei diarrhöischen Zuständen im Kindesalter und bei Erwachsenen, Klin. Wchnschr. **9**:408 (March 1) 1930.

8. Kohlbrugge, J. H. F.: Rohe Apfel-Diät bei diarrhöischen Zuständen im Kindesalter und bei Erwachsenen, Klin. Wchnschr. **9**:408 (March 1) 1930.

9. Mayloth, G.: Zur Vorstellung über die Wirkung der Apfeldiät, Klin. Wchnschr. **10**:1159 (June 20) 1931.

Malyoth does not believe that tannic acid plays an important rôle, as it is present in only 0.068 per cent. Also because tannic acid is dissociated in the small intestine and absorbed, it does not extend far enough to be of value. However, Malyoth said that a protective colloid, such as is present in grated apple, can prevent this absorption, and such a possibility is conceivable. He also disagreed with Heisler's view regarding the effect of fruit acid on the intestinal flora, since it is present in the apple in only 0.59 per cent, and this amount is also hindered in its action by the buffer action of pectin and its salts.

He also thought that possibly other unknown physiologicochemical processes are concerned in the therapeutic effect of the apple diet.

He stated further that another point of importance in this treatment is that the apple diet furnishes sufficient nutrition so as not to impair the important digestive ferments, as is known to occur in the starvation treatment of diarrhea.

I feel that this therapeutic procedure is worthy of notice as it fulfils, in my opinion, the criteria of a satisfactory therapeutic procedure. First, it alleviates the symptoms; second, the results are usually permanent; third, it is safe; fourth, it is practical in the extent that the apples are pleasant to take, easily procurable and economically reasonable.

In conclusion, I can state that seventy cases of various types of diarrhea treated by the administration of raw apple pulp gave excellent results in 88 per cent of the patients. Some of the failures were due to lack of cooperation of the patient or the mother.

The introduction of grated apple pulp represents a valuable addition to the armamentarium in the treatment of diarrheal conditions in children. Its action is not empiric, but involves a number of mechanical, physiologic and chemical principles. The ability to inhibit intestinal peristalsis accounts, in part, for the prompt response following its administration. Of marked importance are its maintenance of nutritional requirements and its power of preventing serious loss of water, which is so much desired in the treatment of diarrhea.

# ASTHMA IN CHILDREN

## AN ANALYSIS OF EIGHTY-FOUR CASES

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The analysis of a group of eighty-four cases of asthma in children who were followed for from six months to three years is presented. All the patients were tested by the intracutaneous method and with extracts made according to the method of Coca. In an analysis of this series, it is found that the age of onset of the first attack of asthma is most frequently in the first three years of life, as is shown in table 1. Forty-one patients had their first attack of asthma before the age of 3 years. In a previous study reported by me,[1] 14 per cent had their first attack in the first year of life, and 19 per cent in the second year. The similarity of these figures for two separate groups indicates the importance of asthma to the pediatrician.

Going further into the histories of these patients, it is interesting to see what illnesses they had before the onset of asthma. My associates and I found that in 67 per cent of the cases measles occurred previous to the first attack. Chickenpox, pertussis and pneumonia were next in frequency of occurrence. Pertussis occurred in only 7 per cent of our cases as compared with 16 per cent in a series reported by Peshkin [2] (table 2).

In the majority of cases the first attack of asthma followed an acute respiratory infection. In the fifty-eight cases in which a definitely reliable history could be obtained, twenty children had asthma after what was called bronchitis and thirty-one after "colds," which were probably acute sinus infections (table 3). Judging from the history and from clinical study of these cases, infection of the respiratory tract or sinuses was, without doubt, the most important single factor in the production of an attack. This was true whether or not the condition was definitely sensitive as shown by cutaneous tests. The picture of these attacks is fairly constant, and the attacks are usually more common in the winter. At the beginning the condition is limited to the nasal mucosa, as evidenced by rhinitis. Subsequently bronchitis with

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1. Chobot, Robert: Incidence of Sinusitis in Asthmatic Children, Am. J. Dis. Child. **39**:257 (Feb.) 1930.

2. Peshkin, M.: Asthma in Children: Incidence and Significance of Various Diseases and Infections, and of Tonsillectomy and Adenoidectomy, Am. J. Dis. Child. **33**:880 (June) 1927.

asthmatic seizures occurs. The attack is severe for a few days, and is generally over in a week. Forty-one of the eighty-four patients had a history of either eczema or urticaria. Of these thirty-three had eczema and eight had urticaria.

TABLE 1.—*Age of Onset of First Attack of Asthma in 83 Cases*

| Age | No. |
|---|---|
| 0– 1 | 14 |
| 1– 2 | 9 |
| 2– 3 | 18 |
| 3– 4 | 6 |
| 4– 5 | 11 |
| 5– 6 | 6 |
| 6– 7 | 5 |
| 7– 8 | 2 |
| 8– 9 | 3 |
| 9–10 | 9 |
| | 83 |

TABLE 2.—*Incidence of Acute Infectious Diseases in the Past History in 58 Cases*

| | No. Cases | Per Cent |
|---|---|---|
| Measles | 39 | 67 |
| Chickenpox | 6 | 10 |
| Pertussis | 5 | 9 |
| Pneumonia | 4 | 7 |
| Diphtheria | 3 | 5 |
| Mumps | 1 | 2 |

TABLE 3.—*Acute Condition Precipitating the First Attack of Asthma*

| Condition | No. Cases |
|---|---|
| Colds | 31 |
| Bronchitis | 20 |
| Pertussis | 3 |
| Tonsillitis and adenoiditis | 2 |
| Pneumonia | 1 |
| Measles | 1 |

TABLE 4.—*Analysis of Cutaneous Reactions*

| Age | No. Sensitive to Food | No. Sensitive to Inhalants |
|---|---|---|
| 1– 2 | 10 | 10 |
| 2– 3 | 20 | 18 |
| 3– 4 | 10 | 9 |
| 4– 5 | 14 | 13 |
| 5– 6 | 11 | 24 |
| 6– 7 | 18 | 20 |
| 7– 8 | 21 | 22 |
| 8– 9 | 4 | 14 |
| 9–10 | 26 | 36 |

As a general rule, it is believed that inhalants play little or no rôle during childhood, and that most sensitivity during early years is due entirely to foods. Stuart and Farnham [3] found that by far the greatest percentage of sensitivity to food is encountered in the second year of

3. Stuart, H. C., and Farnham, H.: Acquisition and Loss of Hypersensitiveness in Early Life, Am. J. Dis. Child. **32**:341 (Sept.) 1926.

life (26 per cent of fifty-seven cases in children). Thereafter, there is a rapid decline; after the eighth year the incidence is negligible. On the other hand, hypersensitiveness to inhalants is infrequent in the first three years (3.5 per cent of eighty-seven cases with positive reactions), and rapidly increases thereafter until the eighth year, after which there is a definite decline. During the fourth and fifth years of life, the frequencies of both types of sensitivity closely approximate each other. Peshkin [4] found food sensitivity reactions in children to be most frequent in the second year. He differed from other observers in that he reported a great frequency of hypersensitiveness to inhalants in his series of children under 14 years of age (98 per cent of the sensitive patients), a larger incidence than that of sensitivity to food in the same

TABLE 5.—*Sensitizations to Inhalants*

| Inhalant | No. Cases | Inhalant | No. Cases |
|---|---|---|---|
| Dust | 66 | Orris | 4 |
| Goat hair | 17 | Cottonseed | 4 |
| Horse dander | 14 | Kapok | 4 |
| Feathers | 14 | Cat | 4 |
| Wool | 11 | Rabbit | 4 |
| Timothy | 9 | Dog | 2 |
| Ragweed | 6 | Flaxseed | 1 |
| Insecticides | 7 | | |

TABLE 6.—*Sensitizations to Foods*

| Food | No. Cases | Food | No. Cases |
|---|---|---|---|
| Cereal | 29 | Beef | 4 |
| Tomatoes | 20 | Mustard | 4 |
| Lima beans | 14 | Orange | 4 |
| Egg | 10 | Peas | 4 |
| Potato | 9 | Nuts | 2 |
| Lamb | 8 | Cocoanut | 1 |
| Chocolate | 7 | Fish | 1 |
| Chicken | 5 | Pork | 7 |
| Milk | 5 | | |

group (71 per cent of the sensitive patients). In our series my associates and I found that sensitivity to inhalants and to foods was parallel until the ninth year, when inhalants definitely established themselves as the predominating causes in the cases studied, as shown in table 4.

Of the eighty-four patients, eighty were definitely cutaneously sensitive. Seventy-two, or 90 per cent, were sensitive to allergens of the inhalant group, and fifty-five, or 68 per cent, were sensitive to foods (figures slightly under those of Peshkin). Table 5 shows the list of inhalants with the number of reactions to each. Dust, goat hair, horse dander and feathers gave the most frequent reactions, and it is interesting to note that there was relative infrequency of sensitivity to the pollens of ragweed and timothy. Why there is not more hay fever in

4. Peshkin, M.: Asthma in Children; Etiology, Am. J. Dis. Child. **31**:763 (June) 1926.

children is still unanswerable. I believe that many of the cutaneous reactions to inhalants obtained in children indicate a potential sensitivity, for clinical experience shows that foods are of the greatest importance, particularly below the age of 3 years. However, when one finds cutaneous reactions to inhalants, a careful check on the environment must be carried out in order to prevent an error of omission. Even though it is most usual to obtain a history of attacks occurring after the ingestion of a food such as eggs, it is not good practice to ignore cutaneous reactions to inhalants even though they have as yet only a potential significance.

In an analysis of table 6, showing the predominant sensitizations to food it is seen that cereals (wheat, barley and rice), eggs and milk were the most common causative foods, which could be checked by a clinical test, namely, feeding of the suspected substance. In the case of a vegetable, such as tomatoes, this could not always be done; hence the incidence must be discounted and explained on the basis of a nonspecific action of the extract when administered intracutaneously. The leguminous vegetables, such as peas and beans, are important factors owing to their high protein content. One outstanding fact observed by many clinicians is the spontaneous loss of sensitivity to food, clinically, as the child grows older. Figures are extremely difficult to obtain, but the loss is seen constantly even though a positive cutaneous reaction may persist. On the other hand, it is important to point out that one occasionally sees patients with a definite history of sensitivity to food in whom it is not possible to elicit a cutaneous reaction. In this type of case it is essential that the history be confirmed and, if the diagnosis is correct, that the food be eliminated from the diet.

One of the most characteristic features of asthma in children is the presence of eosinophils. Normally the eosinophils of the blood may be formed in the bone marrow, and in some animals in the hemolymph nodes.

According to Ringoen [5] many eosinophilic leukocytes are developed in the hemolymph nodes. Schlect and Schwenken [6] studied the eosinophils in anaphylaxis, and found marked eosinophilia of the blood in guinea-pigs after shock, and an infiltration of the pulmonary and bronchial tissues and of the body fluids with eosinophils. Ringoen substantiated these findings, and expressed the belief that the eosinophils in the peritoneal fluids produced by repeated intraperitoneal injections are not produced locally, because of the associated eosinophilia of the blood.

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5. Ringoen, A. R.: Origin of Eosinophilic Leukocytes of Mammals, Folia haemat. **27**:10, 1921.

6. Schlect, H., and Schwenken, G.: Ueber die Beziehungen der Eosinophilie zur Anaphylaxie, Deutsches Arch. f. klin. Med. **108**:405, 1912.

Cooke [7] reported more than 4 per cent of eosinophils in 68 per cent of a series of patients with positive cutaneous tests, and in 47 per cent of those with negative cutaneous reactions. Coates and Ersner [8] reported fifty cases in which the lining of the antrums had been examined. The antral lining in asthmatic patients presented a predominance of eosinophils with some polymorphonuclear leukocytes and lymphocytes. Hansel [9] reviewed one thousand cases studied by him in which nasal and sinus pathologic conditions existed in allergic persons, and he noted the almost constant presence of eosinophils in such tissue.

Fifty-nine cases were studied in this series, and in 57 per cent, or thirty-four, of the patients the eosinophil count was more than 4 per cent. The highest count reported in this group was 18 per cent. My associates and I found that in twenty-seven, or 78 per cent, of the thirty-four cases there were eosinophilia and a concomitant sinus infection. Only seven cases were found in which there was eosinophilia without sinus infection. These figures are shown in table 7.

TABLE 7.—*Occurrence of Eosinophilia and Its Relation to Sinus Infection*

| | Cases |
|---|---|
| Eosinophilia with sinus infection | 27 |
| Sinus infection without eosinophilia | 15 |
| Eosinophilia without sinus infection | 7 |
| Absence of both eosinophilia and sinus infection | 10 |
| Highest eosinophil count | 18% |

One interesting observation may be contributed: One of our patients, a girl of 13, had a badly infected right antrum which was opened and irrigated by Dr. Arthur Nilsen. Prior to operation, the eosinophil count was high, 12 per cent; subsequent to operation it dropped to 2 per cent.

Cooke,[10] studying a group of adults and children, found eosinophilia of the blood in 61 per cent of the asthmatic patients with infection. The maximum eosinophil count was 27 per cent in this group. He inferred that eosinophils can be produced in the tissue of the antrums in the presence of infection, and expressed the belief that if the particular stimulus is sufficiently absorbed to affect the bone marrow eosinophilia of the blood will result. In this way he explained the

7. Cooke, R. H.: Bronchial Asthma, in Diseases of the Respiratory System, in Tice: Practice of Medicine, Hagerstown, Md., W. F. Prior Company, Inc., 1921, sect. 3, chap. 2, p. 500.

8. Coates, G. M., and Ersner, M. S.: Occurrence of Eosinophilia in the Mucous Membrane of the Maxillary Sinus in Asthmatic Patients, Arch. Otolaryng. **11**:158 (Feb.) 1930.

9. Hansel, F. K.: Nose and Sinuses in Allergy, J. Allergy **1**:69, 1929.

10. Cooke, R. A.: Infective Asthma: Indication of Its Allergic Nature, Am. J. M. Sc. **183**:309 (March) 1932.

greater frequency of eosinophil cells in nasal and bronchial membranes than in the blood.

I believe that in asthmatic children a routine differential blood count should be made. Cases in which there is eosinophilia should be carefully checked in order to eliminate a focus of infection, especially in the sinuses, for on the basis of the aforementioned evidence one must look for a stimulus the origin of which is frequently in the paranasal sinuses.

The treatment of sinus infections is to my mind an important problem which has not yet been solved. Removal of tonsils and adenoids is of benefit only when it removes a definite focus and when it enables the sinus to drain freely. In the present series, forty-eight patients, or 69 per cent, had positive roentgenologic findings checked by clinical examination, and twenty-one, or 31 per cent, were normal on roentgen examination. This proportion of positive results is even higher than that in another series of cases reported by me [1] in which 41 per cent of the patients had involvement of the sinuses. I believe that the rise is accounted for by the increasing number of cases in which the condition is suspected and roentgen examination is made.

The anatomic difficulties make conservative treatment imperative in the younger child. The measures vary from simple nasal irrigations to the use of mild silver protein packs and suction. The shallowness of the antrums permits ready drainage, but the constant reinfection makes therapy difficult. In almost all of these cases there is marked lymphoid hyperplasia of the nasopharynx, and this lymphoid tissue is the source of reinfection. In our experience the removal of tonsils and adenoids in the child with established pathologic conditions of the sinuses is of little avail, but should be done as early as possible. To be effective the lymphoid tissue must be removed before the sinus infection has become established. Once the infection is established every means of giving drainage must be employed. In the older child whose second teeth have appeared, puncture with irrigation may be necessary. The use of vaccines is still empiric, and the feeling is becoming more definite that only organisms that on injection can precipitate an attack have a scientific basis for usage. In the treatment of these patients we used a stock catarrhal vaccine, but we felt that whatever benefit resulted was most likely due to the drainage of the sinuses rather than to the effect of the vaccine.

Seventy-two patients have been followed for from six months to three years. Fifty-eight did very well. Seven did only fairly well, and seven did poorly. Those patients designated as doing well were those in whom both the parents and the physician agreed as to the absence of symptoms. I do not use the word "cure" because I do not believe that these cases come under that category, but I can say that fifty-eight (81 per cent) of our patients are symptom-free.

The treatment of the hypersensitive patient depends chiefly on the avoidance of the cause. Frequently this is difficult in children, particularly in the case of sensitivity to milk. We have put our patients who are sensitive to milk on a diet of goat's milk, which is usually well tolerated, but most patients sensitive to cow's milk when tested with goat's milk give a positive cutaneous reaction. The reactions to goat's milk are not as marked, and hence it is tolerated when cow's milk is not. However, two patients with associated eczema became definitely worse when given goat's milk. We have also used sobee, but frequently our patients are sensitive to both milk and cereals and some are not able to tolerate sobee because of its cereal content.

In the treatment of the patients who are sensitive to inhalants, injections of house dust extract were most frequently used. All other inhalants were removed from the child's environment whenever possible. In cases of sensitivity to pollen, injections of the offending pollens were given.

The largest proportion of cases lay in the group in which there were an allergic factor and a concomitant sinus infection. In this group the removal of the offending substances as well as the treatment of the infection is imperative. One form of treatment is useless without the other. The best results are obtained in cases in which because of a family history the child is seen before the establishment of asthma. In such cases the removal of foci and contacts is of immeasurable benefit.

SUMMARY

1. Forty-one per cent of a series of asthmatic children had the first attack of asthma before the age of 3 years. The precipitating cause in the majority of cases was an infection of the respiratory tract.

2. Ninety per cent of the patients gave cutaneous reactions to inhalants, and 68 per cent to foods.

3. Thirty-four of the fifty-nine patients (57 per cent) had eosinophilia of the blood, and of these twenty-seven (78 per cent) had a concomitant sinus infection.

4. Every asthmatic child should have a differential blood count made, and patients with eosinophilia should be carefully studied for foci of infection.

5. Forty-eight patients of a series of sixty-nine had evidence of disturbance in the sinuses, i. e., 69 per cent, a figure higher than that reported by me in a previous study.

6. Fifty-eight of seventy-two patients, or 81 per cent, are symptom-free. The success in treatment depends on removal of the cause, and usually requires the cooperation of a rhinologist.

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# CHEMICAL ACTION OF SODIUM CITRATE AS A CAUSE OF CERTAIN TRANSFUSION REACTIONS

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During the past few years we have gained the impression that occasionally an acutely ill infant is made definitely worse rather than better by a transfusion of citrated blood. Most of these unfavorable results were observed in infants with acute gastro-intestinal disturbances. With one exception, which will be described in more detail, the effects of transfusion could hardly be described as a "transfusion reaction." There were no symptoms similar to those following the injection of incompatible blood, nor was there any suggestion of an allergic reaction, but rather an augmentation of the general unfavorable condition. Citrated transfusions were employed only after careful cross-matching of the donor's and the recipient's serum and cells. Rematching of blood in the cases giving unfavorable results failed to show any indication of incompatibility.

The one instance of a fatality immediately following transfusion convinced us that the transfusion was to blame, and led to the present investigation. A marantic, dehydrated infant on admission to the hospital was given fluids subcutaneously and intraperitoneally and sodium citrate by mouth in doses of 30 cc. of a 5 per cent solution every four hours. Fifteen hours after admission, when the dehydration was only partially overcome, a transfusion of 50 cc. of citrated blood was given. Following the transfusion, the pulse became extremely slow and respirations were slow and gasping and soon ceased entirely. Although the heart continued to beat for several minutes, artificial respiration and the administration of epinephrine and caffeine failed to resuscitate the child, and he died. It was obvious that the transfusion was the immediate cause of death. There was no personal or familial history of allergy, nor was the reaction characteristic of anaphylaxis. The pulse and respiration were unlike those in the reaction to incompatible blood.

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The factor of incompatibility was further ruled out by rematching of the blood after death. There was no sign of agglutination or hemolysis after the preparation had stood for eight hours. The question then arose as to whether the sodium citrate introduced with the blood might have caused the reaction.

The toxicology of sodium citrate has received little attention. Gros [1] and Salant and Hecht [2] described the slowing effect of sodium citrate on the heart, while a paper by Joannides and Cameron [3] showed that rather large doses of sodium citrate introduced intravenously into normal dogs cause general convulsions, salivation, slowing of respiration and cardiac failure. Shelling and Maslow [4] produced convulsions and death in young rabbits by feeding milk containing sodium citrate. They attributed these deaths to a reduction of effective calcium by the absorbed citrate. The same authors reported further experiments in which sodium citrate given intravenously to rabbits produced convulsions and cardiac and respiratory failure. Chemical studies of the blood showed marked changes in the ultrafiltrability of the calcium following the administration of citrate.

The amount of sodium citrate generally used as an anticoagulant has not been found to produce toxic symptoms in normal subjects. Much emphasis has, however, been laid on the toxicity of partially coagulated blood; [5] as a result, the general tendency is in favor of the use of an excess of sodium citrate. For instance, Drinker and Brittingham [5] used as a routine 35 cc. of 8 per cent sodium citrate in transfusions ranging from 250 to 900 cc. Thus in the smaller transfusions these authors introduced approximately a 1 per cent solution of sodium citrate, which is more than three times that needed to prevent coagulation. They stated, however, that this amount of citrate is harmless for adults. As long as transfusions were used chiefly in the treatment of anemia this was probably true, but it may not be the case when sodium citrate is given to recipients whose blood is chemically abnormal in respects other than the reduction of hemoglobin.

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1. Gros, O.: Ueber das Wesen der Oxalsäure-Wirkung auf das Froschherz, Arch. f. exper. Path. u. Pharmakol. **71**:395, 1913.

2. Salant, W., and Hecht, S.: The Influence of Oxalates, Citrates, and Tartrates on the Isolated Heart, Am. J. Physiol. **36**:126, 1915.

3. Joannides, M., and Cameron, A. L.: Citrated Blood Transfusion: An Experimental Study of the Toxicity of Sodium Citrate in Exsanguinated Dogs, J. A. M. A. **82**: 1187 (April 12) 1924.

4. Shelling, D. H., and Maslow, H. L.: The Effect of Sodium Citrate, Acetate, and Lactate on the Ultrafiltrability of Serum Calcium, J. Biol. Chem. **78**: 661, 1928.

5. Drinker, C. K., and Brittingham, H. H.: The Cause of the Reactions Following Transfusion of Citrated Blood, Arch. Int. Med. **23**:133 (Jan.) 1919.

The outstanding chemical effects of sodium citrate are: (1) the removal of calcium ions from solution by the formation of an unionized complex with calcium; (2) the production of a distinctly alkaline solution, since it is a salt of a strong base and a weak acid, and (3) the production of an increase in bicarbonate as a result of combustion in the body. All of these actions tend to reduce the concentration of calcium ions when sodium citrate is injected intravenously, and the symptoms to be expected from an excess of sodium citrate are those due to an acute lack of calcium ions. The most generally recognized of these is tetany. Whether the slowing of the heart may also be attributed directly to the same cause is questionable. However, most investigators have noted this effect following the administration of large doses of sodium citrate and have found the administration of calcium salts the most effective means of preventing this action.

The conditions, therefore, in which one might expect the administration of sodium citrate to be undesirable are those in which there is an actual reduction of total calcium in the body fluids or in which the effect of the calcium is reduced by the presence of some antagonistic substance, or those, such as alkalosis, in which the degree of calcium ionization is diminished. The introduction of blood prevented from clotting by the addition of sodium citrate causes a dilution of the recipient's blood with a solution containing few free calcium ions, while the excess citrate not already combined with the calcium in the donor's blood further reduces its calcium ion concentration.

A condition in children in which the calcium is obviously reduced is infantile tetany. Although transfusions are not indicated for the tetany alone, they are often of great benefit in combating the associated respiratory infection and anemia. Alimentary intoxication in infants with severe diarrhea is commonly treated by repeated transfusions of blood. Dodd, Minot and Casparis [6] have recently shown that this toxic condition is associated with an increase in guanidine in the blood. The antagonism between calcium ions and guanidine compounds has been repeatedly demonstrated,[7] and hence recipients with an increased amount

6. Dodd, K.; Minot, A. S., and Casparis, H.: Guanidine as a Factor in Alimentary Intoxication in Infants, Am. J. Dis. Child. **43**:1 (Jan.) 1932.

7. (*a*) Major, R. H., and Stephenson, W.: Further Studies on the Elevation of Blood Pressure by Guanidine Poisoning, Bull. Johns Hopkins Hosp. **35**:186, 1924. (*b*) Clark, G. A.: Interrelation of Parathyroids, Suprarenals, and Pancreas, J. Physiol. **58**:294, 1923-1924. (*c*) Minot, A. S., and Cutler, J. T.: Guanidine Retention and Calcium Reserve as Antagonistic Factors in Carbon Tetrachloride and Chloroform Poisoning, J. Clin. Investigation **6**:369, 1928. (*d*) Minot, A. S.: The Mechanism of the Hypoglycemia Produced by Guanidine and Carbon Tetrachloride Poisoning and Its Relief by Calcium Medication, J. Pharmacol. & Exper. Therap. **43**:295, 1931.

of guanidine might be expected to be unusually susceptible to a depletion of calcium ions by the introduction of citrate. In children alkalosis is most commonly seen as a result of the persistent vomiting caused by pyloric stenosis or high intestinal obstruction. Transfusions are often desirable before operation in these conditions.

To determine whether sodium citrate is harmful in similar conditions experimentally produced, citrated blood or sodium citrate alone was injected intravenously into dogs with an artificially produced condition of hypocalcemia, hyperguanidinemia or alkalosis. The blood to be transfused was taken from a larger normal dog as donor, received into a flask containing sodium citrate solution and then promptly injected into the recipient. In every case the blood given was shown to be compatible by direct matching of the donor's and the recipient's serum and cells. It is of some interest to note that, though agglutination was seen only occasionally, there was frequently hemolysis of cells which made necessary the finding of a different donor. In these experiments no blood was introduced that showed agglutination or hemolysis with the recipient's serum. The amount of blood transfused into these dogs was the same as would be given to children of equal weight, namely, 10 cc. per pound (500 Gm.) in animals weighing up to 10 pounds (4,500 Gm.), with a maximum transfusion of 250 cc. in animals weighing more. Enough sodium citrate was used to give a final dilution of 0.5 per cent. This is the dilution used in the pediatric ward of the Vanderbilt Hospital and is about the average amount generally used elsewhere. When sodium citrate was given without blood it was similarly diluted with physiologic solution of sodium chloride. To reproduce as nearly as possible experimentally the clinical conditions in which citrated transfusions might be dangerous, latent tetany due to a low calcium content was produced by parathyroidectomy, the guanidine level was increased by the injection of guanidine or by the production of acute destruction of the liver by the administration of carbon tetrachloride,[7c] and alkalosis was produced by the intravenous injection of sodium bicarbonate. Following the transfusion the animals were observed closely for an hour or more. As controls for all three experimental groups similar amounts of sodium citrate both in blood and in physiologic solution of sodium chloride were injected into normal dogs without the production of any untoward symptoms.

## EXPERIMENTATION

*Transfusions of Citrate in Dogs with Lowered Blood Calcium.*—The dogs used as subjects were parathyroidectomized, and the serum calcium was determined at short intervals in order to anticipate the appearance of tetany. When the calcium level had fallen to 7.5 or 8

mg. per hundred cubic centimeters, and before any outspoken symptoms of tetany developed, the transfusion was given. In the majority of cases, when only a part of the blood had been given a marked tremor developed which increased in severity as the injection continued, until clonic convulsions or more commonly a general tonic rigidity with opisthotonos intervened. The pulse became extremely slow, respirations ceased, and the dog became unconscious. After a minute or two the spasm relaxed, respirations began again, and the pulse gradually resumed its normal rate. During the recovery vomiting and frequent defecation occurred. Moderate convulsive twitchings, which could be augmented to a general convulsion by handling of the animal, persisted for an hour or more, depending on the degree of the reduction of calcium in the blood. The reactions varied in severity from those less marked than the ones described to general convulsive seizures in which the animal died within a few minutes. Complete relief from symptoms could be obtained by the intravenous injection of calcium salts. If the blood calcium was raised to a normal or a high level by intravenous injection of calcium before the transfusion was given, no such reaction occurred. Similar symptoms were obtained whether the sodium citrate was given with blood or in physiologic solution of sodium chloride. A protocol typical of the results in seven parathyroidectomized dogs is included.

Dog 24 (Male).—The weight was 7.5 Kg.

July 22: The parathyroid and thyroid glands were removed.

July 23: The serum calcium was 7.7 mg. per hundred cubic centimeters. There was slight hyperexcitability but no tetany. A transfusion of 150 cc. of citrated blood from a compatible donor was given. Tetany developed and became severe during the early part of the transfusion. Later the dog stiffened in general tonic spasm with opisthotonos. The pulse became extremely slow, and respirations ceased. After about two minutes gasping respirations started, which soon became normal, and the pulse gradually resumed a normal rate. Convulsive twitching reappeared and persisted for thirty minutes; a dose of 15 cc. of 7.5 per cent calcium gluconate was given intravenously; all signs of tetany promptly disappeared, and the dog appeared normal.

*Citrated Transfusions in Dogs with Increased Guanidine in the Blood.*—The level of guanidine in the blood of normal dogs is about from 0.3 to 0.4 mg. per hundred cubic centimeters, as determined by our slight modification of the method of Major and Weber.[8] When this level is increased to from 1 to 1.5 mg., marked symptoms of intoxication are seen, unless the subject is adequately protected by calcium.

8. Major, R. H., and Weber, C. J.: The Probable Presence of Increased Amounts of Guanidine in the Blood of Patients with Arterial Hypertension, Bull. Johns Hopkins Hosp. **40**:87, 1927.

The outstanding visible signs of guanidine poisoning are nervous hyperexcitability, manifested by muscle twitching resembling tetany, and gastro-intestinal irritation, evidenced by vomiting and diarrhea. The aim in these experiments was to use subjects with moderately increased guanidine levels but without acute symptoms of intoxication, and to determine whether the reduction of calcium ions by the introduction of citrate would suddenly increase the severity of the symptoms. The hyperguanidinemia was produced in some dogs by the subcutaneous injection of guanidine hydrochloride; in others the increase was allowed to develop endogenously following acute injury to the liver produced by a large dose of carbon tetrachloride.[7d] The transfusions were usually given when a level of from 0.7 to 1 mg. of guanidine per hundred cubic centimeters had been reached. A few subjects had lower and some higher levels than this, but none had muscular twitchings before the transfusion was given. The results of transfusion in these animals were practically identical with those already described. The dogs with the lower level of guanidine showed less severe reactions, while two with the highest concentrations died during the reaction. Again the symptoms could be relieved or prevented by the intravenous administration of calcium. A typical protocol of one of the eight dogs in this group is included.

Dog 14.—The weight was 9.0 Kg. A preliminary sample showed 0.32 mg. of guanidine per hundred cubic centimeters.

July 9, 9 a. m.: Forty-five cubic centimeters of carbon tetrachloride and 30 cc. of alcohol were given by mouth.

July 10, 4 p. m.: The animal was very quiet; there were no tremors. Guanidine was 0.96 mg. per hundred cubic centimeters.

4:15 p. m.: A transfusion of 170 cc. of citrated blood from a compatible donor was given. There was marked tremor at the end of the transfusion, which developed into violent general clonic convulsions which persisted for from five to ten minutes and then gradually subsided during the next half hour. The respiratory and pulse rates were slow at the end of the transfusion.

*Citrated Transfusions in Dogs with Alkalosis.*—The reactions seen following the injection of citrated blood into animals previously made more alkaline by the administration of sodium bicarbonate were not as severe as those seen in the other two conditions described. The recipient dog's total blood calcium level was normal, and before the transfusion the action of the calcium was interfered with only by a depression of the degree of ionization due to the alkalosis. In these experiments the alkalosis was not carried to the point of producing signs of tetany. The alkali reserve was raised to from 80 to 90 per cent by volume, and the $p_H$ of the blood was from 7.6 to 7.7. Following or during transfusion, there was a rapid onset of moderate and typical tetany, which persisted

until the chemical composition of the blood was more nearly normal. None of these animals died. This experiment was carried out on eight dogs. A typical protocol follows.

Dog 15.—The weight was 11.3 Kg. The preliminary sample of blood, *A*, showed: $p_H$, 7.41; carbon dioxide content, 44.2 per cent by volume, and alkali reserve, 42.2 per cent by volume.

Oct. 27, 9 a. m.: Ten grams of sodium bicarbonate in 140 cc. of 7 per cent solution was given intravenously. There was slight tremor at the end of the injection, but this soon disappeared and the dog appeared normal.

9:40 a. m.: Sample *B* was drawn before transfusion. The dog appeared perfectly normal. The specimen showed: $p_H$, 7.64; carbon dioxide content, 98.6 per cent by volume, and alkali reserve, 95.9 per cent by volume.

9:45 to 9:55 a. m.: A transfusion of 150 cc. of citrated blood from a compatible donor was given. Respirations became slow and gasping; the pulse was not markedly slowed. Marked twitching of muscles and general clonic convulsions of moderate severity persisted for about twenty minutes and then gradually disappeared.

A common factor in the three conditions in which the effect of sodium citrate has been studied is a moderate depression of effectual calcium before the transfusions were given, due either to actual lack of calcium ions or to the presence of an antagonistic substance. The administration of blood or of physiologic solution of sodium chloride containing sodium citrate precipitated more or less severe reactions in all three conditions.

In order to show that the effects observed were due to sodium citrate in amounts that were excessive for the experimental conditions produced, larger amounts of sodium citrate (from 150 to 225 mg. per kilogram) were injected into normal dogs. Reactions were produced that were similar to those seen following smaller doses in the abnormal subjects. Usually the first symptoms were twitching of the muscles and increased visible peristalsis followed by frequent defecation. During the early convulsive movements the pulse rate increased, but as the injection continued the slowing effect of the citrate on the heart became marked. The pulse dropped to from 20 to 40 beats per minute, but was of fair quality. At this stage respirations ceased; the tetany that had increased from the early muscle twitching to a general tonic spasm disappeared, and the dogs lay unconscious. If untreated, some of the subjects died without regaining consciousness; others began to breathe, the pulse rate gradually increased, and recovery seemed complete in from about twenty to thirty minutes. If rather large doses of calcium chloride or calcium gluconate were given intravenously shortly before the injection of sodium citrate, no symptoms, or at the most only mild tetany, developed. If calcium salts were given by vein during the height of the reaction, there was an immediate increase in pulse rate,

respirations were resumed, and recovery was much more prompt, the dogs appearing normal three or four minutes after they had been unconscious.

COMMENT

We have shown that dogs with certain chemical abnormalities of the blood are unusually susceptible to sodium citrate. They show severe and sometimes fatal reactions following the injection of the amounts of citrate ordinarily used as an anticoagulant in blood transfusions. It is probable that children with similar chemical changes in the blood would have the same increased susceptibility to sodium citrate. Though our studies on guanidine had not been initiated at the time when we first had the impression that citrated transfusions were sometimes harmful, poor results often had been seen in conditions that we now believe to be associated with increased guanidine in the blood.[6] Guanidine is known to have toxic effects other than the production of nervous hyperexcitability and gastro-intestinal irritation. Among these are disturbances in carbohydrate metabolism brought about, as indicated by Staub [9] and Minot,[7d] by interference with the normal metabolism of lactic acid. This condition as well as the nervous symptoms are relieved by calcium.[7d] We have now found that the increase in the guanidine level that is associated with severe diarrhea is persistent until normal fluid equilibrium has been reestablished; and, since calcium medication does not decrease the guanidine but merely combats its effects, it seems obvious that any reduction of active calcium by the introduction of citrate might increase the toxic action of the guanidine even in cases in which no marked reaction is precipitated. This may account for our earlier impression that children with acute gastro-intestinal indigestion were sometimes made worse by transfusions of citrate. The one fatality that occurred in a child was preceded by a depression of respiration and a very slow pulse—symptoms that were always seen in the more severe reactions in dogs.

In view of the experience of Shelling and Maslow [4] following the feeding of sodium citrate to rabbits, it seems to make no difference whether the sodium citrate reaches the blood stream through gastro-intestinal absorption or by direct injection. This suggests that the oral administration of sodium citrate to combat acidosis may also be dangerous for children with gastro-intestinal indigestion. Though we have no direct experimental data on this point, we have given up the oral use of sodium citrate, since the importance of calcium in combating guanidine has been recognized. During the last year transfusions of citrated

9. Staub, H.: Experimentelle Studien über Synthalinwirkung, Ztschr. f. klin. Med. **107**:607, 1928.

blood to infants with diarrhea have been preceded by an intravenous injection of calcium gluconate, and unfavorable effects have not been observed.

Since this danger from citrated transfusions can be overcome so easily, the disadvantage is outweighed by the obvious advantages of the use of this method of transfusion in children. Owing to the well known dangers associated with the introduction of partially coagulated blood, the prevention of the effects of citrate on the recipient by the previous injection of calcium appears safer than a reduction of the amount of citrate used. The intravenous administration of calcium salts is not always free from danger, but we have found that the slow injection of from 3 to 10 cc. of a 10 per cent solution of calcium gluconate is a safe procedure.

SUMMARY

Infants with certain chemical abnormalities of the blood may be harmed rather than benefited by transfusions of citrated blood even when no incompatibility or allergy can be demonstrated. Considerable evidence that the introduction of sodium citrate is the cause of the trouble has been obtained from experiments on animals. Unfavorable reactions have been produced in dogs with low values for blood calcium, with increased guanidine in the blood and with alkalosis by the introduction of an ordinary citrated transfusion or of similar amounts of sodium citrate in saline solution. Though no symptoms of reaction were produced by the injection of equal amounts into normal control animals, the same effect could be produced by much larger doses of citrate. The reaction is typical of an acute lack of calcium, and is relieved or prevented by the administration of calcium salts. The results indicate the importance of readjustment of abnormal chemical conditions of the blood before the giving of citrated transfusions. When this is impossible, calcium therapy is an effective means of prevention or relief of the type of reaction that has been described. Similar danger associated with the absorption of sodium citrate from the gastro-intestinal tract is also discussed.

# UREA CLEARANCE IN NORMAL AND IN DEHYDRATED INFANTS

## RENAL FUNCTION IN INTESTINAL INTOXICATION

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A large number of investigators have measured the end-products of nitrogen metabolism in the blood and their excretion in the urine in health and in disease as an aid in evaluating the functional capacity of the kidneys. Ambard and Weill [1] were the first to relate the concentration of urea in the blood to its concentration in the urine and to the urinary volume as expressed by "Ambard's coefficient." Addis and his collaborators [2] showed that more constant results could be obtained if, under standard conditions of fluid intake, the rate of urea excretion was measured as $\frac{\text{urea in 1 hour's urine}}{\text{urea in 100 cc. of blood}}$. They introduced the assumption, and supported it by animal experiments, that the weight of the kidney is proportional to surface area rather than body weight, which was used by Ambard. Under Addis' standard conditions the volume of urine in normal persons was above 2 cc. per minute.

Van Slyke and his co-workers [3] supplied an explanation for the constancy of Addis' ratio. They observed that above a certain urinary

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1. Ambard, L., and Weill, A.: Les lois numériques de la sécrétion rénale de l' urée et du chlorure de soude, J. de physiol. et de path. gén. **14**:753, 1912.

2. Addis, T., and Watanabe, C. K.: A Method for the Measurement of the Urea Excreting Function of the Kidneys, J. Biol. Chem. **28**:251, 1916. Addis, T.: Renal Function and the Amount of Functioning Tissue: The Ratio: $\frac{\text{Urea in One Hour's Urine}}{\text{Urea in 100 Cc. of Blood}}$ After Giving Urea and Water, Arch. Int. Med. **30**:378 (Sept.) 1922. Taylor, F. B.; Drury, D. R., and Addis, T.: The Regulation of Renal Activity: VIII. The Relation Between the Rate of Urea Excretion and the Size of the Kidneys, Am. J. Physiol. **65**:55, 1932.

3. Austin, J. H.; Stillman, E., and Van Slyke, D. D.: Factors Governing the Excretion Rate of Urea, J. Biol. Chem. **46**:91, 1921. Möller, E.; McIntosh, J. F., and Van Slyke, D. D.: Studies of Urea Excretion: II. Relationship Between Urine Volume and the Rate of Urea Excretion by Normal Adults, J. Clin. Invesigation **6**:427, 1928; IV. Relationship Between Urine Volume and the Rate of Urea Excretion by Patients with Bright's Disease, ibid. **6**:485, 1928; III. The Influence of Body Size on Urea Output, ibid. **6**:467, 1928.

volume (range from 1.7 to 2.5 cc., average 2 cc.), the excretion of urea proceeded at maximum speed. This quantity was termed the augmentation limit. They showed that above the augmentation limit the quantity of blood cleared from urea per minute is proportional to the volume of urine, whereas below this point it is proportional to the square root of the volume. Accordingly, for the calculation of the clearance, the following equations were used:

$$C_m = \frac{U}{B} V; \quad C_s = \frac{U}{B} \times \sqrt{V},$$

$C_m$ is the maximum clearance; $C_s$, the standard clearance; U, the concentration of urea in the urine in milligrams per hundred cubic centimeters; B, the concentration of urea in the blood in milligrams per hundred cubic centimeters, and V, the volume of urine excreted per minute.

The advantages of Van Slyke's method are: (1) it can be used even though very small amounts of urine are secreted; (2) the figures, if expressed in percentage of the normal clearance, afford a fairly reliable index of the quantity of functioning renal tissue; (3) no preparations are required except an accurate timing of the specimens, and (4) if a correction for surface area is made, the method can be applied to the measurement of renal function in children.

The procedure followed by Van Slyke and his co-workers appeared to be sufficiently simple to apply to the study of the renal function of infants suffering from intestinal intoxication. Although the etiology of this condition is still unknown, the restoration of normal water metabolism in the tissues and of kidney secretion has become of prime importance in its symptomatic treatment. As early as 1918, Schloss [4] studied renal function in intestinal intoxication and found a decrease in the phenolsulphonphthalein output and an increase in Ambard's constant as compared with values in normal infants. In the light of the newer knowledge of the disease, it seemed interesting to study this problem with a different method. The following questions merit consideration: 1. Does Van Slyke's formula apply to normal infants? 2. How great is the clearance in infants suffering from intestinal intoxication? 3. What factors are responsible for the disturbance of renal function in intestinal intoxication as detected by the urea clearance?

## METHODS

Nine female infants who were free from nutritional disturbances and whose urine did not contain pathologic elements were studied. Most of them were under the care of the foster-home department of the New York Nursery and Child's

4. Schloss, O. M.: Intestinal Intoxication in Infants: The Importance of Impaired Renal Function, Am. J. Dis. Child. **15**:165 (March) 1918.

Hospital and were free from disease during observations. Their ages varied between 2 and 11½ months (table 1). They received their last feedings of milk at 6:00 a. m.; the observation was usually begun at 9:00 a. m., and they received no additional milk until the end of the period. During this time the subjects were kept under constant supervision on a metabolism mattress. The infants were catheterized at the beginning of the observation, the time was noted, and the specimen was discarded. One-half hour later, the first sample of blood was taken, either by venipuncture or from the heel. About one hour after the first catheterization, the initial specimen of urine was obtained. The time was noted, and the specimen was measured. Any urine voided during the hour was retained under oil and added to the catheterized specimen. This procedure was repeated for the second sample of blood and urine and sometimes for a third sample at hourly intervals. If a stool was passed with the urine, or urine was lost, the entire observation was repeated. In several instances, a few drops of urine were lost (tables 1 and 2). In two cases (cases 8 and 9) urea was given dissolved in milk. Whenever water was administered, it was given directly after catheterization. The intake of water ranged from 2 to 4 ounces (59.2 to 118.4 cc.).

The same procedure was followed in eight cases of intestinal intoxication (two boys and six girls). The ages ranged from 1 to 11 months. Four of the eight patients died. In the male subjects, the urine of the first spontaneous voiding was discarded and the time noted. Blood was taken about one-half hour after each spontaneous urination. In case 6 (that of a girl) spontaneous voiding occurred twice before an hour had passed. These samples were used despite the shorter period. In many of the cases the treatment with subcutaneous injections of physiologic solution of sodium chloride and intravenous dextrose solutions had been started several hours before the beginning of the observation. No milk was given during this period, but water was offered in the same way as to the normal infants. No urea was given to any subject suffering from intestinal intoxication.

Urea in the urine was determined by the Van Slyke-Cullen urease method.[5] Ammonia was estimated by Folin's method as modified by Pincussen.[6] Urea in the blood was determined by Leiboff's method[7] and by Van Slyke's gasometric micromethod,[8] depending on the amount of blood available. The blood for the latter method was obtained by puncture of the heel, since capillary blood contains the same amount of urea as venous blood.[9] Clotting of the blood was prevented by the use of heparin. All determinations were made immediately following the withdrawal of specimens. Urea added to urine was recovered to 98 per cent. Leiboff's method gives slightly higher values than the aeration method. Control analyses of the blood to which urea had been added resulted in 100.7 and 95 per cent recoveries with the methods of Leiboff and Van Slyke, respectively. In a few instances, the results obtained with the micromethod on known solutions

5. Van Slyke, D. D., and Cullen, G. E.: A Permanent Preparation of Urease, and Its Use for Rapid and Accurate Determination of Urea, J. A. M. A. **62**:1558 (May 16) 1914.

6. Pincussen, L.: Mikromethodik, ed. 2, Leipzig, Georg Thieme, 1923, p. 21.

7. Leiboff, S. L., and Kahn, B. S.: A Rapid and Accurate Method for the Determination of Urea in Blood, J. Biol. Chem. **83**:347, 1929.

8. Van Slyke, D. D.: Determination of Urea by Gasometric Measurement of the Carbon Dioxide Formed by the Action of Urease, J. Biol. Chem. **73**:695, 1927.

9. Johnston, C.: Comparison of Urea Nitrogen Content of Cutaneous and Venous Blood by Micro-Gasometric Analysis, J. Clin. Investigation **9**:209, 1930.

TABLE 1.—*Urea Excretion in Normal Infants*

| Case | Name; Sex; Age | Observed Height, Cm.; Weight, Kg.; Surface Area, Sq.M. | Observed Height, Cm.; Ideal Weight, Kg.; Ideal Surface Area, Sq.M. | U Urine Urea Nitrogen, Mg. per 100 Cc. | Urine Ammonia Nitrogen, Mg. per 100 Cc. | B Blood Urea Nitrogen, Mg. per 100 Cc. | V Urine Volume, Cc. per Min. | Urine Volume Corrected for Body Size, Cc. per Min. $V \times \frac{1.73}{S.A.}$ | Urine Volume Corrected for Body Size, Cc. per Min. $V \times \frac{1.73}{\text{Ideal S.A.}}$ | Uncorrected Clearances, Cc. Blood per Min. $\frac{U \times V}{B}$ Observed Clearance* | Uncorrected Clearances, Cc. Blood per Min. $\frac{U \times \sqrt{V}}{B}$ Standard Clearance Calculated for V = 1 from Observations Below Augmentation Limit | Clearances Corrected for Body Size, Cc. Blood per Min. $\frac{U\left(V \times \frac{1.73}{S.A.}\right)}{B}$ Observed Clearance | Clearances Corrected for Body Size, Cc. Blood per Min. $\frac{U \times \sqrt{V \times \frac{1.73}{S.A.}}}{B}$ Standard Clearance Calculated for V = 1 from Observations Below Augmentation Limit | Clearances Corrected for Ideal Body Size, Cc. Blood per Min. $\frac{U\left(V \times \frac{1.73}{S.A.}\right)}{B}$ Observed Clearance | Clearances Corrected for Ideal Body Size, Cc. Blood per Min. $\frac{V \times \sqrt{V \times \frac{1.73}{S.A.}}}{B}$ Standard Clearance Calculated for V = 1 from Observations Below Augmentation Limit |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | K. B. | 60 | 60 | 435.06 | 16.52 | 12.5 | 0.283 | 1.897 | 1.682 | 9.8 | 18.5 | .... | 48.0 | .... | 45.2 |
| | ♀ | 4.2 | 5.62 | 311.14 | 8.74 | 12.66 | 0.426 | 2.856 | 2.533 | 10.5* | .... | 70.2 | .... | 62.3 | .... |
| | 5 mos. | 0.258 | 0.291 | | | | | | | | | | | | |
| 2 | D. D. | 56.5 | 56.5 | 538.44 | 254.1 | 8.9 | 0.058 | 0.452 | 0.383 | 3.5 | 14.6 | .... | 40.7 | .... | 37.4 |
| | ♀ | 4.18 | 4.91 | | | | | | | | | | | | |
| | 2 mos. | 0.223 | 0.263 | | | | | | | | | | | | |
| 3 | H. M. | 64.5 | 64.5 | 353.64 | 46.76 | 11.17 | 0.391 | 2.255 | 2.0 | 12.4 | ... | .... | 48.75 | .... | 46.0 |
| | ♀ | 5.34 | 7.0 | 214.34 | 37.1 | 10.25 | 0.693 | 3.997 | 3.547 | 14.5* | .... | 83.6 | .... | 74.2 | .... |
| | 3 mos. 10 days | 0.3 | 0.338 | | | | | | | | | | | | |
| 4 | V. P. | 67.75 | 67.75 | 437.36 | 21.84 | 17.73 | 0.742 | 3.888 | 3.556 | 18.3* | .... | 95.9 | .... | 87.7 | .... |
| | ♀ | 6.23 | 7.73 | 188.72 | 12.32 | 13.08 | 1.119 | 5.864 | 5.362 | 16.1* | .... | 84.6 | .... | 77.4 | .... |
| | 8 mos. | 0.33 | 0.361 | | | | | | | | | | | | |
| 5 | A. B. | 70.0 | 70.0 | 868.42 | 68.46 | 15.7 | 0.206 | 0.943 | 0.925 | 11.4 | 24.9 | .... | 53.7 | .... | 53.2 |
| | ♀ | 8.01 | 8.35 | | | | | | | | | | | | |
| | 11½ mos. | 0.378 | 0.385 | | | | | | | | | | | | |
| 6 | E. H. | 59.0 | 59.0 | 552.4 | 40.6 | 14.7 | 0.212 | 1.427 | 1.283 | 8.0 | 17.3 | .... | 44.8 | .... | 42.7 |
| | ♀ | 4.31 | 5.54 | 245.84 | 16.24 | 14.5 | 0.642 | 4.32 | 3.88 | 10.85* | .... | 73.2 | .... | 65.8 | .... |
| | 6 mos. | 0.257 | 0.286 | | | | | | | | | | | | |
| 7 | B. W. | 67.0 | 67.0 | 452.06 | 30.1 | 12.24 | 0.328 | 1.79 | 1.63 | 12.1* | .... | 66.1 | .... | 60.2 | .... |
| | ♀ | 5.73 | 7.14 | 273.56 | 13.72 | 13.58 | 0.5 | 2.73 | 2.49 | 10.05* | .... | 55.0 | .... | 50.1 | .... |
| | 7 mos. | 0.317 | 0.348 | | | | | | | | | | | | |
| 8 | R. S.† | 59.5 | 59.5 | 1,297.94 | 126.56 | 14.11 | 0.075 | 0.534 | 0.457 | 6.9 | 25.2 | .... | 67.2 | .... | 62.5 |
| | ♀ | 3.75 | 5.39 | 1,041.44 | 81.67 | 13.42 | 0.057‡ | 0.402‡ | 0.344‡ | 4.4‡ | 18.5‡ | .... | 49.3‡ | .... | 45.8‡ |
| | 2½ mos. | 0.243 | 0.284 | 313.84 | 15.44 | 26.29 | 0.792 | 5.64 | 4.82 | 9.5* | .... | 67.3 | .... | 57.5 | .... |
| 9 | P. S.§ | 58.0 | 58.0 | 1,009.77 | 38.36 | 21.41 | 0.148 | 0.974 | 0.928 | 6.99 | 18.2 | .... | 46.5 | .... | 45.4 |
| | ♀ | 4.66 | 5.29 | 1,149.96 | 25.48 | 22.4 | 0.167 | 1.099 | 1.047 | 8.57 | 21.0 | .... | 53.6 | .... | 52.3 |
| | 3 mos. | 0.263 | 0.276 | 267.68 | 10.08 | 19.49 | 0.781 | 5.14 | 4.897 | 10.7* | .... | 70.6 | .... | 67.2 | .... |

* Maximum clearance values observed when V was above the augmentation limit (see text).
† One gram of urea was given at the beginning of the second period.
‡ A few drops of urine were lost.
§ One gram of urea was given thirty minutes before the first catheterization.

of urea were unexpectedly low. No explanation for this discrepancy was evident, since the variables, urease and $p_H$ were adequately controlled.

For calculation of the urea clearance, the volumes of urine were corrected for surface area, Van Slyke's factor $\frac{1.73}{S.A.}$ being used, in which 1.73 represents the average surface area of an adult, and S.A. the observed surface area of the subject. If this correction is applied, the formulas take this form:

$$C_s = \frac{U}{B} \times \sqrt{V \times \frac{1.73}{S.A.}} \text{ and } C_m = \frac{U}{B} \times V \times \frac{1.73}{S.A.}$$

Surface area was calculated from body height and weight according to Du Bois and Du Bois' formula.[10]

From six to seven observations are necessary to obtain a reliable estimate of the augmentation limit with the procedure of Van Slyke. We did not feel justified in withdrawing this number of samples of blood from one infant in a short period. Furthermore, the intake of fluid of an infant cannot be regulated as strictly as in adults or in older children. Realizing the foregoing limitations, we nevertheless, in all cases in which two or more determinations were made, attempted to calculate the augmentation limit following Van Slyke's method. According to the result, the clearances were calculated as maximum or standard clearance. If only one determination was done, $C_m$ or $C_s$ was calculated if the corrected volume of urine per minute was above or below 2, respectively. In some cases, however, in which duplicate determinations were available, both clearances were found to be either standard or maximum clearances.

## RESULTS

The results in normal infants are summarized in table 1. It can be seen that the values for standard clearance vary between 40.7 and 67.2 cc. of blood. The average of 50.46 represents 93.4 per cent of 54 cc., the average figure observed in adults. As might be expected, the values for maximum clearance show better agreement with Van Slyke's figures than the results obtained with small volumes of urine (standard clearance). They vary between 55 and 95.9 cc., with an average of 73 cc. The average value represents 97.3 per cent of the normal figure of 75 cc. in adults. The results indicate that the standard and maximum clearances for normal infants are slightly less than the values found by Van Slyke for adults and children, but are of similar magnitude.

Van Slyke's calculations of the surface area for adults are based on Du Bois' height-weight formula. Although the ideal weight of an infant of a given height varies markedly in normal babies, we have calculated the results not only for actual surface area, but also on the basis of ideal surface area with the aid of the tables of Woodbury.[11]

10. Du Bois, D., and Du Bois, E. F.: Clinical Calorimetry: X. A Formula to Estimate the Approximate Surface Area if Height and Weight Be Known, Arch. Int. Med. **17**:863 (June) 1916.

11. Woodbury, R. M.: Statures and Weights of Children Under Six Years of Age, U. S. Dept. Labor, Children's Bureau, 1921, Bull. 87.

It can be seen in table 1 that the clearance values for ideal surface area are lower than those based on observed surface area. This diminution also holds for the infants suffering from intestinal intoxication.

An attempt was made to determine the augmentation limit (cases 1, 3, 6, 8 and 9). The results vary greatly: 2.35, 3.10, 2.86, 1 and

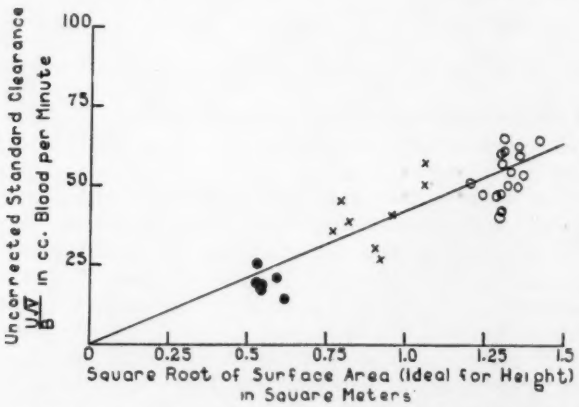


Chart 1.—Relation of surface area to uncorrected standard clearance values. In this chart and chart 2 the solid circle represents infants, our series; x, children, Van Slyke's series,[8] and the open circle, adults, Van Slyke's series.

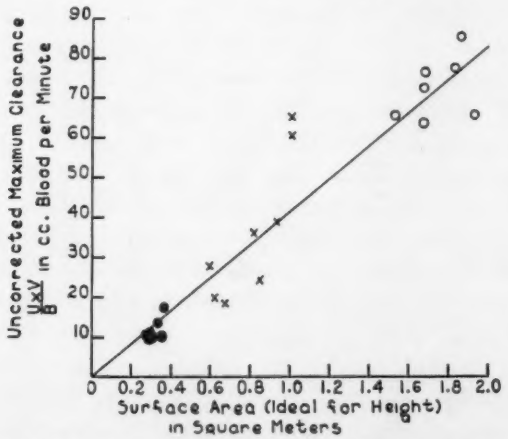


Chart 2.—Relation of surface area to uncorrected maximum clearance values.

2.26, respectively, with an average of 2.31 cc. If in cases 4 and 7, in which two determinations were made, the augmentation limit was calculated on the assumption that the lower volume of urine represented standard clearance, it was found that the volume of urine in both instances exceeded the augmentation limit as calculated. This indicated, according to Van Slyke's definition, that both values were maximum

TABLE 2.—*Urea Excretion in Infants with Intestinal Intoxication*

| Case | Name; Sex; Age | Serum: $CO_2$, per Cent by Volume | Serum: $p_H$ | Serum: NaCl, Mg. per Cent | Observed Height, Cm.; Weight, Kg.; Surface Area, Sq.M. | Observed Ht., Cm.; Ideal Wt., Kg.; Ideal Surface Area, Sq.M. | U Urine Urea Nitrogen, Mg. per 100 Cc. | Urine Ammonia Nitrogen, Mg. per 100 Cc. | B Blood Urea Nitrogen, Mg. per 100 Cc. | V Urine Volume, Cc. per Min. | $V \times \frac{1.73}{S.A.}$ Urine Volume Corrected for Body Size, Cc. per Min. | $V \times \frac{1.73}{\text{Ideal } S.A.}$ Urine Volume Corrected for Ideal Body Size, Cc. per Min. | Clearances Corrected for Body Size: Observed Clearance, Cc. Blood per Min. $U\left(V \times \frac{1.73}{S.A.}\right)/B$ | Clearances Corrected for Body Size: Observed Clearance, Cc. Blood per Min. $U \times \sqrt{V \times \frac{1.73}{S.A.}}/B$ | Clearance in per Cent of Normal: $C_m$ | Clearance in per Cent of Normal: $C_s$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | A. T. | .... | .... | ... | 42.0 | .... | 1,073.9 | 230.7 | 33.39 | 0.02 | 0.203 | ..... | .... | 14.46 | .... | 26.8 |
| | ♀ | | | | 2.81 | .... | 850.1 | 119.4 | 30.38 | 0.086 | 0.878 | ..... | .... | 26.22 | .... | 48.6 |
| | 27 days | | | | 0.17 | .... | | | | | | | | | | |
| 2 | E. M. | .... | .... | ... | 65.0 | 65.0 | 1,251.9 | 241.6 | 21.63 | 0.067 | 0.372 | 0.341 | .... | 35.31 | .... | 65.4 |
| | ♀ | | | | 5.71 | 7.0 | 1,227.7 | 194.3 | 14.85 | 0.069 | 0.382 | 0.351 | .... | 51.26 | .... | 94.9 |
| | 6 mos. | | | | 0.313 | 0.34 | 299.9 | 48.6 | 14.70 | 0.47 | 2.62 | 2.40 | 53.9 | ..... | 71.9 | .... |
| 3 | G. J. | .... | .... | ... | 51.0 | 51.0 | 353.4 | 84.0 | 29.8 | 0.131 | 1.146 | 1.045 | .... | 12.69 | .... | 23.5 |
| | ♀ | | | | 3.0 | 3.7 | 262.3 | 57.5 | 30.05 | 0.242 | 2.119 | 1.931 | .... | 12.74 | .... | 23.6 |
| | 1 mo. 10 days | | | | 0.198 | 0.217 | | | | | | | | | | |
| | 1 mo. 25 days | | | | 51.0 | 51.0 | 580.3 | 189.0 | 21.4 | 0.117 | 1.03 | 0.9 | .... | 27.5 | .... | 50.9 |
| | | | | | 2.90 | 4.0 | 422.5 | 104.2 | 21.1 | 0.193 | 1.70 | 1.48 | 34.0 | ..... | 45.3 | .... |
| | | | | | 0.196 | 0.225 | | | | | | | | | | |
| 4 | J. M. | 28.5 | 7.32 | ... | 57.0 | 57.0 | 357.0 | 121.8 | 18.02 | 0.162 | 1.12 | 1.047 | .... | 21.0 | .... | 38.9 |
| | ♂ | | | | 4.30 | 5.0 | 254.8 | 76.2 | 23.14 | 0.313 | 2.16 | 2.022 | 23.8 | ..... | 31.7 | .... |
| | 3 mos. | | | | 0.25 | 0.268 | | | | | | | | | | |
| 5 | R. v.Cl. | .... | .... | ... | 48.5 | 48.5 | 1,066.7 | 282.1 | 17.0 | 0.034 | 0.306 | 0.29 | .... | 34.7 | .... | 64.3 |
| | ♂ | | | | 3.09 | 3.5 | 1,082.1 | 264.8 | 19.47 | 0.044 | 0.391 | 0.374 | .... | 34.8 | .... | 64.4 |
| | 1 mo. 5 days | | | | 0.194 | 0.205 | | | | | | | | | | |
| 6 | O. G.* | 17.3† | 7.17 | 754 | 59.75 | 59.75 | 81.00 | 98.7 | 45.6 | 0.04 | 0.263 | 0.239 | .... | 0.91 | .... | 1.7 |
| | ♀ | 37.1† | 7.35 | 614 | 4.54 | 5.70 | 88.2 | 105.0 | 37.3 | 0.012 | 0.075‡ | 0.068 | ... | 0.65 | .... | 1.2 |
| | 6 mos. | | | | 0.265 | 0.292 | | | | | | | | | | |
| | 6 mos. 9 days | | | | 59.75 | 59.75 | 176.12 | 40.04 | 28.25 | 0.28 | 1.88 | 1.658 | .... | 8.54 | .... | 15.8 |
| | | | | | 4.26 | 5.70 | 148.26 | 42.7 | 33.5 | 0.303 | 2.04 | 1.794 | .... | 6.33 | .... | 11.7 |
| | | | | | 0.257 | 0.292 | 197.79 | 42.56 | 33.5 | 0.193 | 1.3 | 1.143 | .... | 6.73 | .... | 12.5 |
| 7 | B. G. | 14.7 | .... | 688 | 48.5 | 48.5 | 480.5 | 104.7 | 38.8 | 0.085 | 0.888 | 0.715 | .... | 11.64 | .... | 10.5 |
| | ♀ | | | | 2.10 | 3.5 | 513.3 | 68.9 | 39.1 | 0.032‡ | 0.332 | 0.268 | .... | 7.56 | .... | 6.8 |
| | 1 mo. 25 days | | | | 0.165 | 0.205 | 461.2 | 68.7 | 39.1 | 0.127 | 1.334 | 1.072 | .... | 13.62 | .... | 12.2 |
| 8 | J. B. | 15.0† | 7.08 | 701 | 52.5 | 52.5 | 142.8 | 13.44 | 20.4 | 0.733 | 6.68 | 5.47 | 38.3 | ..... | 62.4 | .... |
| | ♂ | 20.0† | 7.27 | 660 | 2.62 | 4.10 | 185.5 | 28.6 | 21.45 | 0.50 | 4.39 | 3.60 | 31.1 | ..... | 50.6 | .... |
| | 3½ mos. | | | | 0.19 | 0.232 | | | | | | | | | | |

* Phenolsulphonphthalein test, 17 per cent in two hours.
† Determinations not done on day of experiment.
‡ Few drops of urine lost.

It can be seen in table 1 that the clearance values for ideal surface area are lower than those based on observed surface area. This diminution also holds for the infants suffering from intestinal intoxication.

An attempt was made to determine the augmentation limit (cases 1, 3, 6, 8 and 9). The results vary greatly: 2.35, 3.10, 2.86, 1 and

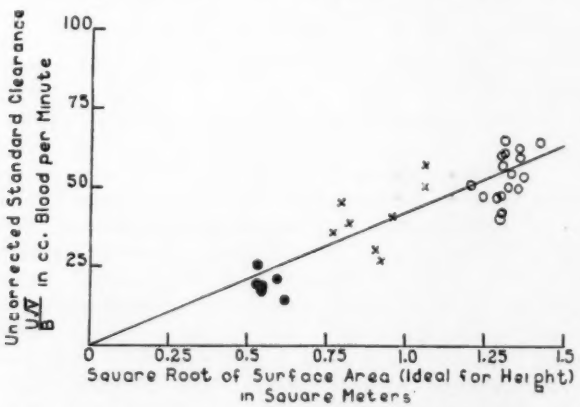


Chart 1.—Relation of surface area to uncorrected standard clearance values. In this chart and chart 2 the solid circle represents infants, our series; x, children, Van Slyke's series,[8] and the open circle, adults, Van Slyke's series.

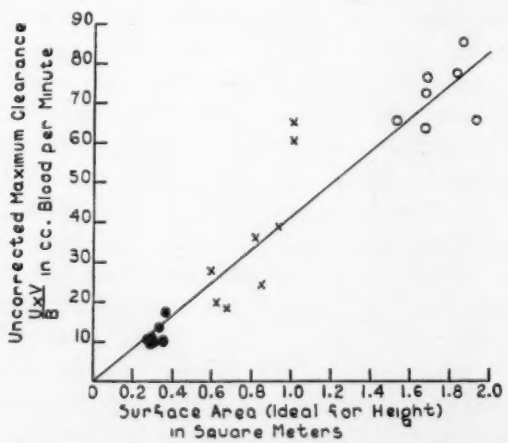


Chart 2.—Relation of surface area to uncorrected maximum clearance values.

2.26, respectively, with an average of 2.31 cc. If in cases 4 and 7, in which two determinations were made, the augmentation limit was calculated on the assumption that the lower volume of urine represented standard clearance, it was found that the volume of urine in both instances exceeded the augmentation limit as calculated. This indicated, according to Van Slyke's definition, that both values were maximum

TABLE 2.—*Urea Excretion in Infants with Intestinal Intoxication*

| Case | Name; Sex; Age | Serum: $CO_2$, per Cent by Volume | Serum: $p_H$ | Serum: NaCl, Mg. per Cent | Observed Height, Cm.; Weight, Kg.; Surface Area, Sq.M. | Observed Ht., Cm.; Ideal Wt., Kg.; Ideal Surface Area, Sq.M. | U Urine Urea Nitrogen, Mg. per 100 Cc. | Urine Ammonia Nitrogen, Mg. per 100 Cc. | B Blood Urea Nitrogen, Mg. per 100 Cc. | V Urine Volume, Cc. per Min. | $V \times \frac{1.73}{S.A.}$ Urine Volume Corrected for Body Size, Cc. per Min. | $V \times \frac{1.73}{Ideal\ S.A.}$ Urine Volume Corrected for Ideal Body Size, Cc. per Min. | Clearances Corrected for Body Size: Observed Clearance, Cc. Blood per Min. $U\left(V \times \frac{1.73}{S.A.}\right)/B$ | Clearances Corrected for Body Size: Observed Clearance, Cc. Blood per Min. $U \times \sqrt{V \times \frac{1.73}{S.A.}}/B$ | Clearance in per Cent of Normal: $C_m$ | Clearance in per Cent of Normal: $C_s$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | A. T. ♀ 27 days | .... | .... | ... | 42.0<br>2.81<br>0.17 | ....<br>....<br>.... | 1,073.9<br>850.1 | 230.7<br>119.4 | 33.39<br>30.38 | 0.02<br>0.086 | 0.203<br>0.878 | .....<br>..... | ....<br>.... | 14.46<br>26.22 | ....<br>.... | 26.8<br>48.6 |
| 2 | E. M. ♀ 6 mos. | .... | .... | ... | 65.0<br>5.71<br>0.313 | 65.0<br>7.0<br>0.34 | 1,251.9<br>1,227.7<br>299.9 | 241.6<br>194.3<br>48.6 | 21.63<br>14.85<br>14.70 | 0.067<br>0.069<br>0.47 | 0.372<br>0.382<br>2.62 | 0.341<br>0.351<br>2.40 | ....<br>....<br>53.9 | 35.31<br>51.26<br>..... | ....<br>....<br>71.9 | 65.4<br>94.9<br>.... |
| 3 | G. J. ♀ 1 mo. 10 days | .... | .... | ... | 51.0<br>3.0<br>0.198 | 51.0<br>3.7<br>0.217 | 353.4<br>262.3 | 84.0<br>57.5 | 29.8<br>30.05 | 0.131<br>0.242 | 1.146<br>2.119 | 1.045<br>1.931 | ....<br>.... | 12.69<br>12.74 | ....<br>.... | 23.5<br>23.6 |
| | 1 mo. 25 days | | | | 51.0<br>2.90<br>0.196 | 51.0<br>4.0<br>0.225 | 580.3<br>422.5 | 189.0<br>104.2 | 21.4<br>21.1 | 0.117<br>0.193 | 1.03<br>1.70 | 0.9<br>1.48 | ....<br>34.0 | 27.5<br>..... | ....<br>45.3 | 50.9<br>.... |
| 4 | J. M. ♂ 3 mos. | 28.5 | 7.32 | ... | 57.0<br>4.30<br>0.25 | 57.0<br>5.0<br>0.268 | 357.0<br>254.8 | 121.8<br>76.2 | 18.02<br>23.14 | 0.162<br>0.313 | 1.12<br>2.16 | 1.047<br>2.022 | ....<br>23.8 | 21.0<br>..... | ....<br>31.7 | 38.9<br>.... |
| 5 | R. v.Cl. ♂ 1 mo. 5 days | .... | .... | ... | 48.5<br>3.09<br>0.194 | 48.5<br>3.5<br>0.205 | 1,066.7<br>1,082.1 | 282.1<br>264.8 | 17.0<br>19.47 | 0.034<br>0.044 | 0.306<br>0.391 | 0.29<br>0.374 | ....<br>.... | 34.7<br>34.8 | ....<br>.... | 64.3<br>64.4 |
| 6 | O. G.* ♀ 6 mos. | 17.3†<br>37.1† | 7.17<br>7.35 | 754<br>614 | 59.75<br>4.54<br>0.265 | 59.75<br>5.70<br>0.292 | 81.00<br>88.2 | 98.7<br>105.0 | 45.6<br>37.3 | 0.04<br>0.012 | 0.263<br>0.075‡ | 0.239<br>0.068 | ....<br>.... | 0.91<br>0.65 | ....<br>.... | 1.7<br>1.2 |
| | 6 mos. 9 days | | | | 59.75<br>4.26<br>0.257 | 59.75<br>5.70<br>0.292 | 176.12<br>148.26<br>197.79 | 40.04<br>42.7<br>42.56 | 28.25<br>33.5<br>33.5 | 0.28<br>0.303<br>0.193 | 1.88<br>2.04<br>1.3 | 1.658<br>1.794<br>1.143 | ....<br>....<br>.... | 8.54<br>6.33<br>6.73 | ....<br>....<br>.... | 15.8<br>11.7<br>12.5 |
| 7 | B. G. ♀ 1 mo. 25 days | 14.7 | .... | 688 | 48.5<br>2.10<br>0.165 | 48.5<br>3.5<br>0.205 | 480.5<br>513.3<br>461.2 | 104.7<br>68.9<br>68.7 | 38.8<br>39.1<br>39.1 | 0.085<br>0.032‡<br>0.127 | 0.888<br>0.332<br>1.334 | 0.715<br>0.268<br>1.072 | ....<br>....<br>.... | 11.64<br>7.56<br>13.62 | ....<br>....<br>.... | 10.5<br>6.8<br>12.2 |
| 8 | J. B. ♂ 3½ mos. | 15.0†<br>20.0† | 7.08<br>7.27 | 701<br>660 | 52.5<br>2.62<br>0.19 | 52.5<br>4.10<br>0.232 | 142.8<br>185.5 | 13.44<br>28.6 | 20.4<br>21.45 | 0.733<br>0.50 | 6.68<br>4.39 | 5.47<br>3.60 | 38.3<br>31.1 | .....<br>..... | 62.4<br>50.6 | ....<br>.... |

* Phenolsulphonphthalein test, 17 per cent in two hours.
† Determinations not done on day of experiment.
‡ Few drops of urine lost.

clearances. Our determinations in each case, however, are too few to draw general conclusions concerning the augmentation limit in normal infants.

In chart 1, the individual values for observed standard clearance are plotted against the square root of observed surface area. These values approximate the smoothed curve derived by Van Slyke from his average values for adults and children. In chart 2, the individual figures for observed maximum clearance are plotted against observed surface area. These values fall slightly below the respective lines for the maximum clearance of adults and children. From these two figures, we may conclude that Van Slyke's formulas can be applied to the calculation of urea clearance in infants.

The results obtained in infants suffering from intestinal intoxication are summarized in table 2. Data on the chemical composition of the blood, when determined, are given in the table. They correspond with those usually found in cases of intestinal intoxication: low carbon dioxide, low $p_H$ and low, normal or increased chlorine. The highest value for urea nitrogen observed was 45.6 mg. per hundred cubic centimeters. In none of these subjects did the volume of urine reach 1 cc. per minute despite attempts to force fluids during the period of observation. The clearances of some infants varied considerably in successive periods, as one might expect, but in others the results obtained in individual periods showed surprisingly good agreement.

In all except two cases (cases 2 and 5) the observed maximum clearances were considerably diminished. In case 6, in which practically no urine was excreted, the clearance was only from 1 to 2 per cent of the normal average value.

An attempt was made to determine the augmentation limit. The latter could be established in cases 2, 3 (second determination) and 4. The values were 1.72, 1.7 and 1.4 cc., respectively, with an average of 1.6 cc. of urine. An attempt to calculate the augmentation limit in the other cases was unsuccessful, as the volumes of urine in all determinations on the same subject represented standard clearances except in case 8, in which both measurements were maximum clearances.

It appears from the results that both standard and maximum clearances in dehydrated infants are usually below normal, being markedly so in some cases.

## COMMENT

Our results indicate that Van Slyke's formula for urea clearance is applicable to infants. There are, however, certain difficulties connected with the application of the method to infants. The first one is the intake of fluid. In order to obtain a maximum function of the kidney, large amounts of fluid must be taken. In only one normal

subject was an output of urine of more than 1 cc. per minute obtained. The second difficulty was the collection of specimens. In our first attempts male infants were used, but the dependence on spontaneous voidings in these subjects made this procedure time-consuming and the withdrawal of samples of blood difficult to time. For this reason only female infants, who were catheterized at hourly intervals, were used in our later studies. Failure to empty the bladder completely and difficulty in the collection of small amounts of urine may be responsible for greater variation in the augmentation limit in these subjects; these factors have been discussed by Van Slyke for older children.

From our data, which admittedly are insufficient, it seems that the augmentation limit is more variable in normal infants than in adults. This may be dependent on extrarenal factors, as the water content of an infant is much greater than at a later age. However, the average augmentation limit was in agreement with that found by Van Slyke for children and adults. In three dehydrated infants the augmentation limit was found slightly lower than in the normal infants. It is not possible to draw any conclusions from these few observations, but it is interesting that in patients with chronic nephritis Van Slyke and his co-workers [3] found the augmentation limit lower than in normal adults.

Another difficulty in the evaluation of the results for urea clearance in infants is its dependence on ideal surface area. It has already been mentioned that the weight and height of normal infants vary greatly, and that the calculation of surface area according to Du Bois' formula is based on these two measurements. For this reason, the results obtained both with observed and ideal surface area are shown in table 1. There are only few direct determinations of the surface area of infants available in the literature. According to Frontali,[12] the result of direct determination of the surface area of infants is 7.9 per cent lower than the values obtained with the Du Bois formula. Scammon and his co-workers [13] found the mean relative deviation of measured values of children under 41 pounds (18,597.6 Gm.) of weight, compared with the Du Bois formula, to be ± 7.3 per cent. The Du Bois formula was used in this study because Van Slyke's calculations for adults were derived from it and because to our knowledge no better formula is at present available.

The same difficulties are encountered when Addis' ratio is calculated in those cases in which the corrected output of urine per minute is above

12. Frontali, G.: Misurazioni dirette di superficie corporea nel bambino, Riv. di clin. pediat. **25**:241, 1927.

13. Boyd, E.; Scammon, R. E., and Lawrence, D.: The Determination of Surface Area in Living Children, Proc. Soc. Exper. Biol. & Med. **27**:445, 1930. Boyd, E., and Scammon, R.: The Relation of Surface Area to Body Weight in Postnatal Life, ibid. **27**:449, 1930.

the augmentation limit. The normal figure for the ratio is 50 in young adults. In six normal infants, Addis' ratio varied between 38.5 and 52.2, with an average of 46.4. These results indicate that Addis' ratio may be applied to infants if the correction for surface area is used.

The diminution of standard and maximum clearances in cases of intestinal intoxication theoretically may be due either to renal or extrarenal causes or to a combination of both. A failure of the kidney itself may be due to pathologico-anatomic changes, to functional changes or to a combination of both. That lesions of the kidneys do occur in intestinal intoxication has been stated by many observers. In two of our cases (cases 4 and 7), postmortem examinations were performed. Slight granular degeneration of the convoluted tubules of the kidneys with some swelling of the cells was present (Dr. Ferris and Dr. Woodward). The investigations of MacKay and MacKay [14] and Van Slyke [15] have shown that a marked rise in blood urea usually does not occur unless at least 50 per cent of the renal tissue has been destroyed. Cases 6 and 7 show a considerable rise of urea nitrogen in the blood, and many of Schloss' cases and those of others reported in the literature show still higher values. Although the pathologic changes do not seem to indicate 50 per cent of destruction of the kidneys, we find a marked diminution of the clearance.

In the absence of pathologic changes, extrarenal changes or functional changes in the kidneys themselves may be responsible for the diminished clearance. Such functional changes in the kidneys seem to be closely related to extrarenal factors,[16] and therefore the latter will be considered first.

Dehydration of the blood and tissues seems to be the most important of the extrarenal factors. Schloss has shown that in cases of intestinal intoxication with low phenolsulphonphthalein tests and high Ambard's coefficients, there is often an increase in the blood concentration measured by total nitrogen, specific gravity, corpuscular volume and total solids. In his opinion, "this increase in concentration, however, was

14. MacKay, E. M., and MacKay, L. L.: The Relation Between the Blood Urea Concentration and the Amount of Functioning Renal Tissue, J. Clin. Investigation **4**:127, 1927.

15. Van Slyke, D. D.; McIntosh, J. F.; Möller, E.; Hannon, R. R., and Johnston, C.: Studies of Urea Excretion: VI. Comparison of the Blood Urea Clearance with Other Measures of Renal Function, J. Clin. Investigation **8**:357, 1930.

16. Czerny, A., and Keller, A.: Das Kindes Ernährung, ed. 1, Leipzig, Franz Deuticke, 1910, vol. 2, p. 152. Schloss (footnote 4). Howland, J., and Marriott, W. McKim: Acidosis Occurring with Diarrhea, Am. J. Dis. Child. **11**:309 (May) 1916. Marriott, W. McKim: Some Phases of the Pathology of Nutrition in Infancy, ibid. **20**:461 (Dec.) 1920. Bessau, G.: Ueber enterale Infektion, Monatschr. f. Kinderh. **22**:280, 1921. Finkelstein, H.: Lehrbuch der Säuglingskrankheiten, ed. 3, Berlin, Julius Springer, 1924, p. 152.

insufficient to account for the increase in non-protein nitrogen." He came to the conclusion that the deficient elimination of the kidney is dependent to a notable degree on the negative water balance. He quoted Bang,[17] who found that when dogs are deprived of water, the blood shows a rise in nonprotein nitrogen. More recently, MacKay and MacKay[18] found that in rabbits that were deprived of food and water for three days, there was only a slight decrease of the Addis ratio. In rabbits that were starved and dehydrated by one intravenous injection of 50 per cent sucrose, only a slight decrease took place, whereas in those that received repeated injections of sucrose, a decrease of about 50 per cent occurred. In their opinion, the main cause of the rise of urea in the blood is an increased formation of urea from an accelerated tissue catabolism, owing to starvation and lack of fluid. In human beings water hunger also increases the breaking down of protein (Straub[19] and Schiff[20]). The feeding of large amounts of urea to animals and human beings, however, leads to an increased excretion of urea, and, consequently, the clearance remains normal (Addis and Drury[21] and Drury[22]), as in our experiments and in those of simple starvation of MacKay and MacKay.

In the dehydration induced by intestinal intoxication of infants, other changes take place in the body which may lead to a disturbance of renal function. An increase of the viscosity of the blood has been found in some of these subjects (Rosenbaum[23]). This would support Schloss' assumption that the "blood colloids may be increased to such a degree that they exert an osmotic pressure greater than the pressure in the glomerular capillaries." The consequence would be anuria or oliguria. In addition, we know that in many instances the blood flow[24]

17. Bang, I.: Untersuchungen über den Reststickstoff des Blutes, Biochem. Ztschr. **72**:119, 1915.

18. MacKay, L. L., and MacKay, E. M.: Increased Blood Urea Concentration of Extrarenal Origin, Am. J. Physiol. **70**:394, 1924.

19. Straub, W.: Einfluss der Wasserentziehung auf den Stoffwechsel, Ztschr. f. Biol. **38**:537, 1899.

20. Schiff, E.: Wirkung eingeschränkter Wasserzufuhr auf den N- und Cl-Umsatz und die Ammoniakausscheidung, Monatscher. f. Kinderh. **15**:593, 1919.

21. Addis, T., and Drury, D. R.: The Rate of Urea Excretion: V. The Effect of Changes in Blood Urea Concentration on the Rate of Urea Excretion, J. Biol. Chem. **55**:105, 1923.

22. Drury, D. R.: The Rate of Urea Excretion: The Effect of Very High Blood Urea Concentrations on the Rate of Urea Excretion, J. Biol. Chem. **55**:113, 1923.

23. Rosenbaum, S.: Beiträge zur Säuglings-Intoxikation: V. Wasserverarmung und Wasserzufuhr, Monatschr. f. Kinderh. **28**:289, 1924.

24. Utheim, Kirsten: A Study of the Blood and Its Circulation in Normal Infants and in Infants Suffering from Chronic Nutritional Disturbances, Am. J. Dis. Child. **20**:366 (Nov.) 1920.

and the blood volume [25] are diminished in intestinal intoxication. The diminished blood volume and retarded blood flow would lead to a decrease of the normal supply of blood to the kidney. This not only reduces the fluid supply of the kidney necessary for the production of urine, but at the same time diminishes the oxygen supply of the kidney.

Decreased oxygenation of renal tissue and of other tissues leads to an accumulation of acids in the body. Acidosis was present in all of our cases that were examined and in most of Schloss' cases. Clinical experience has shown that dehydration precedes acidosis in most cases, and that, if the dehydration is removed, the acidosis will disappear in most instances.[26] On the other hand, the kidney can be damaged by the feeding of acid both in infants and in animals. Infants who are fed concentrated hydrochloric acid milk or calcium chloride frequently show casts and albumin in the urine [27] analogous to those frequently found in babies suffering from intestinal intoxication and infants who have been dehydrated experimentally by an insufficient supply of water.[28] Renal tissue is sensitive to decreased oxygenation,[29] and this, together with the acidosis, may cause functional changes that lead to a diminution of the excretion of urea in intestinal intoxication.

It is probable from these observations that the primary prerenal deviation of water (Fishberg [30]) due to diarrhea, vomiting and insufficient intake of fluid leads to dehydration with its sequences of diminished oxygen and water supply of the kidney. This in turn produces an acidosis of the blood and of the tissues, including renal tissues. It seems that dehydration is the primary cause of diminished renal function. A vicious circle is established which can often be removed by restoring normal water metabolism in the body.[31]

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25. Utheim (footnote 24). Darrow, D. C., and Buckman, T. E.: The Volume of the Blood: II. The Volume of the Blood and Concentration of Crystalloids and Electrolytes in Dehydration and Edema, Am. J. Dis. Child. **36**:248 (Aug.) 1928. McIntosh, R.; Kajdi, L., and Meekers, D.: Blood Volume and Plasma Electrolyte Changes in the Dehydration of Infants, J. Clin. Investigation **9**:333, 1930.

26. Schloss (footnote 4). Footnote 16.

27. Feuchtwanger, A., and Lederer, M.: Zur Frage der Entstehung von Harnzylindern bei Säuglingen, Jahrb. f. Kinderh. **112**:7, 1926.

28. Schiff, E., and Bayer, W.: Das Nierensyndrom, Jahrb. f. Kinderh. **108**:158, 1925.

29. Barcroft, J., and Brodie, T. G.: The Gaseous Metabolism of the Kidney, J. Physiol. **32**:18, 1904; **33**:52, 1905-1906.

30. Fishberg, A. M.: Hypertension and Nephritis, Philadelphia, Lea & Febiger, 1931, p. 39.

31. Hoag, L. A., and Marples, E.: Acid-Base Status in Dehydration Accompanying Diarrhea in Infants: Effect of Treatment with Parenteral Fluids, Am. J. Dis. Child. **42**:291 (Aug.) 1931. Karelitz, Samuel: Treatment of Toxicosis with the Aid of a Continuous Intravenous Drip of Dextrose Solution, Am. J. Dis. Child. **42**:781 (Oct.) 1931.

It would be interesting if similar observations could be made in other diseases in which dehydration is an outstanding symptom. In pyloric stenosis, intestinal obstruction, acute and chronic nephritis, so-called pyelitis and diabetes mellitus, dehydration and oliguria often are pronounced, and an increase in nonprotein and urea nitrogen is frequently observed. It is possible that in these conditions, which are characterized by excessive loss of water from the body (prerenal deviation), the urea clearance may be diminished, and the mechanism of decreased renal function may be analogous to that described in intestinal intoxication.

SUMMARY

The urea clearance of nine normal infants corrected for surface area was found to agree with the values observed by Van Slyke and his co-workers and Addis and his collaborators for older children and adults. This would indicate that renal function measured by the ability to excrete urea is as well developed in infants as in later life.

In infants suffering from severe diarrhea and vomiting (intestinal intoxication), the urea clearance is often greatly reduced. The possible causes of this reduction have been discussed. In the absence of pathologico-anatomic lesions of the kidneys, dehydration and its concomitant effects on body fluids and renal tissue are considered to be the most important factors leading to a reduced urea clearance.

Reference has been made to the application of these results to other clinical conditions associated with dehydration. In the presence of dehydration, a low urea clearance may lead to false conclusions regarding renal damage.

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# ENTERAL ADMINISTRATION OF SCARLATINAL FILTRATE TOXIN

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ST. LOUIS

Parenteral injections of scarlatinal streptococcus filtrate toxin either subcutaneously or intramuscularly are followed in a short time by a loss of skin sensitivity to the toxin. Peters and Allison,[1] by spraying a solution of the toxin every second day for five weeks on the nasal mucosa, reported that of sixty-one children so treated, negative reactions to the Dick test developed in twenty-two and in twenty-four others the skin reaction was "much reduced" at the end of this period. In the present paper are reported the results of a series of experiments in which the toxin was administered in various ways through the gastro-intestinal tract and the effect on skin sensitivity observed.

## MATERIALS AND METHODS

The children studied were patients at the Shriner's Hospital for Crippled Children who were undergoing orthopedic treatment, and who were apparently free from infections. Skin tests were made with standard toxin from the United States Hygienic Laboratory, containing 35,000 skin test doses (STD) per cubic centimeter. In every test a quantitative determination of the skin sensitivity was made by the intradermal injection of 2, 20 and 50 STD of toxin. All tests were read after twenty-four hours.

The scarlatinal streptococcus products administered were all prepared in the Eli Lilly Biological Research Laboratories under the supervision of Mr. F. G. Jones. The products used were as follows:

1. Gabritschewsky vaccine. This was a seventy-two hour veal broth culture of scarlatinal streptococcus, killed by heating for one hour at 56 C. It contained 50,000 million bacteria and 35,000 STD of toxin per cubic centimeter.

2. Enteric streptococcus pills, each of which contained 20,000 million streptococci killed at 56 C. and dried.

3. Etenric toxin pills prepared with toxin concentrated by the method of Hartley [2] and Pulvertaft [3] and containing 30,000 STD in each.

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From the Department of Pediatrics, Washington University School of Medicine, and the St. Louis Children's Hospital.

1. Peters, B. A., and Allison, S. F.: Intranasal Immunization Against Scarlet Fever, Lancet **1**:1035 (May 18) 1929.

2. Hartley, P.: Experiments on the Purification and Concentration of Scarlet Fever Toxin, Brit. J. Exper. Path. **9**:259 (Oct.) 1928.

3. Pulvertaft, R. S.: On the Concentration and Purification of Streptococcal Toxin, Brit. J. Exper. Path. **9**:276 (Oct.) 1928.

4. Toxin suppositories prepared with toxin concentrated in the same way and containing 30,000 STD in each suppository.

5. Concentrated toxin purified and concentrated ten times according to the method of Ando, Kurauchi and Nishimura,[4] and containing approximately 500,000 STD per cubic centimeter.

In the experimental observations that follow, groups of five or six children, each of whom had a strongly positive reaction to 2 STD of standard scarlatinal filtrate toxin, were used. Rarely did a child serve as a subject in more than one experiment. Each experiment lasted from four to six weeks, and during this time the antigen was administered; from six to eight skin tests, with 2, 20 and 50 STD of toxin, were made to determine any change in skin sensitivity. All scarlatinal streptococcus products given orally were administered about 6:30 a. m., one-half hour before breakfast. The enteric coated pills, filtrate or vaccine were followed by a glass of water. The children who were given rectal suppositories or instillations received them later in the day, after the rectum had been emptied either spontaneously or by enema.

## EXPERIMENTAL DATA

EXPERIMENT 1.—*Toxin Subcutaneously.*—The first series of tests comprised a control group of six children, from 4 to 13 years old, with positive reactions to 2 STD, who were given small quantities of toxin subcutaneously, and the subsequent change in skin sensitivity followed by skin tests done twice weekly during the following month. Each was given 500 STD on the first, 1,500 STD on the second and 3,500 STD on the fifth day of the experiment. All of the children gave negative reactions to 2 STD on the ninth day. In one of these, the test was negative to 50 STD, but the others at this time had positive, although weaker, reactions to 20 and 50 STD. By the eighteenth day, two others had become negative to 50 STD, three remained positive with the larger quantities of toxin (20 and 50 STD), and one of these again showed a weak reaction to 2 STD. These results remained constant in the tests during the following two weeks of the experiment.

The results in this group showed that the toxin used was antigenic when introduced in relatively small quantities parenterally; that the skin sensitivity was reduced in all the children in whom injection was made; that the resulting loss of skin sensitivity was more marked in some than in others, and that the change appeared usually within two weeks and persisted for at least two weeks longer.

EXPERIMENT 2.—*Enteric Pills Containing Toxin, Given Orally.*—Each of six children with strongly positive skin reactions to 2 STD was given one pill containing 30,000 STD of toxin twice weekly for four weeks. Skin tests made during this time and for two weeks afterward showed practically no change in the skin sensitivity of five of the children. In one child, the reaction to 2 STD became negative on the eighteenth day and remained negative during the following month, although the reactions to the larger doses of toxin (from 20 to 50 STD) continued to be positive but were somewhat weaker.

EXPERIMENT 3.—*Enteric Pills Containing Killed Streptococci, Given Orally.*—Another group of six children, with strongly positive reactions to 2 STD, was given enteric coated pills of killed scarlatinal streptococci twice weekly for four weeks. Each pill contained 30 billion organisms. Tests showed no change in skin sensitivity during the administration of the pills and for the following two weeks.

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4. Ando, K.; Kurauchi, K., and Nishimura, H.: Studies on the "Toxins" of Hemolytic Streptococci: III. On the Dual Nature of Dick Toxin, J. Immunol. **18**:3 (March) 1930.

EXPERIMENT 4.—*Large Amounts of Filtrate Toxin Orally.*—These six children were given a broth filtrate containing 35,000 STD per cubic centimeter every fourth day for three weeks. The first three doses were small, and the last three were 20 cc. each, a total of 70 cc. being given to each child (about 2,500,000 STD). In none was the skin sensitivity altered, either during the time the filtrate was given or for two weeks afterward.

EXPERIMENT 5.—*Gabritschewsky's Vaccine Orally.*—One group of five children skin sensitive to 2 STD of toxin and another group of five with negative reactions to 2 STD but positive to 20 STD received Gabritschewsky's vaccine at the same intervals and amounts as the children in the preceding experiment. The vaccine contained 50,000 million streptococci and 35,000 STD of toxin per cubic centimeter, so that the total quantities received by each child were approximately 3,500,000,000,000 streptococci and 2,500,000 STD of filtrate toxin. No child in either group showed any but minor variations in skin sensitivity in tests done during the administration of the vaccine or for the following two weeks.

EXPERIMENT 6.—*Gabritschewsky's Vaccine Orally in Buffered Milk.*—Twenty cubic centimeters of vaccine identical with that used in experiment 5, with 200 cc. of milk and 10 Gm. of sodium bicarbonate, was given daily for five days to each of five children having strongly positive skin reactions to 2 STD of toxin. Tests done on the seventh, eleventh, eighteenth and twenty-fifth days after the first treatment showed no change in the skin sensitivity to toxin. Each of these children had taken orally 3,500,000 STD of toxin and 5 million million streptococci.

From the foregoing experiments, it was concluded that the ingestion of massive doses of scarlatinal filtrate toxin and of killed scarlatinal streptococci produced no alteration in skin sensitivity to the toxin. Since the parenteral introduction of relatively small quantities of the filtrate produced a fairly prompt reduction in skin sensitivity, it seemed apparent that none of the ingested antigen was absorbed unchanged into the circulation. Even when the antigen was given in enteric coated pills or in milk buffered with sodium bicarbonate in an attempt to secure its passage unaltered into the intestine, the result was the same.

Observations on the permeability of the rectal mucosa for the filtrate toxin were then made. All rectal injections were small because of the uncertainty that larger volumes would be retained.

EXPERIMENT 7.—*Rectal Application of Suppositories Containing Toxin.*—Each of six children with strongly positive skin tests to 2 STD of toxin was given one suppository twice weekly for four weeks. Each suppository contained 30,000 STD of toxin. Skin tests done weekly showed in all children a decrease in skin sensitivity to 2 STD of toxin after the third week of the experiment. In two children the test with this amount was negative, or a very faint reaction of 5 mm. diameter occurred, while in the other four the reactions were very faint, although they measured from 5 to 10 mm. in diameter. The tests with 20 STD showed no change. The reduction in skin sensitivity in these children seemed definite although slight.

EXPERIMENT 8.—*Introduction of Concentrated Toxin by Rectum.*—In this final experiment, rectal injections of a concentrated toxin were made in an effort to secure absorption of unaltered antigen through the mucosa. Five children, each of whom had a strongly positive reaction with 2 STD of the toxin, were tested once weekly for five weeks. During the first sixteen days of this period each child received eight rectal injections of a streptococcus filtrate toxin containing 50,000 STD per cubic centimeter. One dose of 1 cc., four doses of 2 cc. and three doses of 4 cc. were given. On the eighteenth day, tests showed a slight reduction in skin sensitivity to 2 STD, evidenced by a fainter reaction, but all were still weakly positive. On the twentieth and twenty-first days, 1 cc. of a concentrated toxin

containing 500,000 STD per cubic centimeter was given, 2 cc. on the twenty-third and 4 cc. on the twenty-fourth day of the experiment. By the twenty-eighth day, skin tests with 2 STD were negative in each child and again on the thirty-fourth day. In one child the reactions to 20 and 50 STD of toxin remained negative after the twenty-fourth day, but in the other four these larger amounts of toxin continued to give positive reactions, although in two, they were faint.

## COMMENT AND SUMMARY

The oral administration of large quantities of scarlatinal streptococcus filtrate toxin and of killed hemolytic streptococci was followed by no demonstrable reduction in skin sensitivity to the filtrate toxin, even when several million million skin test doses of toxin and a similar number of bacteria were given. In some instances the antigens were given in enteric pills or in milk buffered with sodium bicarbonate in an effort to secure their passage unchanged into the intestine, without producing any change in the skin sensitivity. Since the parenteral introduction of small amounts of the filtrate produces a readily demonstrable reduction in the skin reactivity to filtrate toxin, it was apparent that no ingested antigen had passed through the gastric or intestinal mucosa in the children studied. It is reasonable to conclude, therefore, that streptococci and their products swallowed with food or during pharyngeal infections play no part in the development of immunity. Apparently the absorption of antigenic substance which results in loss of skin sensitivity and the development of antitoxin occurs ordinarily only from inflammatory foci infected by streptococci.

When a highly concentrated preparation of streptococcus filtrate toxin was introduced rectally, the skin sensitivity to toxin was constantly decreased, so that the reaction to 2 STD became negative. This was interpreted to mean that a certain amount of toxin had been absorbed through the rectal mucosa into the circulation. The skin sensitivity to larger quantities (20 and 50 STD) of toxin, however, was relatively little changed, indicating that the actual amount of antigen reaching the circulation was limited. It is possible that by the continued use of rectal instillations of concentrated filtrate toxin a loss of skin sensitivity to larger amounts of toxin could be produced.

## CONCLUSIONS

The oral administration of killed scarlatinal hemolytic streptococci and of filtrate toxin produced no reduction in skin sensitivity to toxin, indicating that such substances are not absorbed by the gastric or intestinal mucosa. Following the rectal instillation of highly concentrated toxin, there was a constant decrease in skin sensitivity, although the skin remained sensitive to larger quantities of the toxin, showing a definite but limited absorption of filtrate toxin through the rectal mucosa.

# RESULTS OBTAINED FROM THE USE OF VARIOUS TUBERCULIN TESTS

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The various diagnostic tuberculin tests are the outcome of the introduction of tuberculin by Koch in 1890. In 1907 Pirquet evolved the cutaneous scratch method, and in the same year Moro developed the "percutaneous" or inunction method, and Wolff-Eisner and Calmette the conjunctival modification. The intracutaneous test of Mantoux, now so widely used, was described in 1908. In 1909, Hamburger and Monti added the "Stich" or "subcutaneous" test. No other innovations are noted until 1916, when Craig [1] described a "multiple puncture test," an adaptation of Hill's technic for smallpox vaccination. In 1927 Stewart [2] proposed a "single puncture" test, which yielded results identical with those obtained with the Pirquet test.

For a number of years the Pirquet test, because of the simplicity of its technic, enjoyed the widest popularity. Comparison of results with the cutaneous and the Mantoux methods demonstrated the unquestioned superiority of the intracutaneous method. On the basis of a comparative study conducted in the children's medical division of Bellevue Hospital, Smith [3] discarded the cutaneous in favor of the intracutaneous test. Dickey and Seitz [4] likewise advised against the use of the Pirquet test. Fenger, Matill and Phelan [5] encountered only 10 per cent positive reactions to the Pirquet test in a group of Minnesota school children, and regarded this excessively low incidence as evidence of its unre-

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From the Medical Department, National Jewish Hospital, Denver.

1. Craig, D. A.: Cutaneous Tuberculin Test by Puncture with a Solid Needle, J. A. M. A. **67**:1227 (Oct. 21) 1916.

2. Stewart, C. A.: Pirquet Test; Comparison of Scarification and Puncture Methods of Application, Am. J. Dis. Child. **35**:388 (March) 1928.

3. Smith, C. H.: Tuberculin Skin Reactions, Am. J. Dis. Child. **38**:1137 (Dec.) 1929.

4. Dickey, L. B., and Seitz, R. P.: Incidence of Tuberculous Infection as Based on 3,500 Intracutaneous Tuberculin Tests, Am. Rev. Tuberc. **23**:3 (Jan.) 1931.

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liability. Forbes and Green,[6] in a series of 131 cases, found 6.17 per cent more positive reactions with the Mantoux than with the Pirquet test. On the other hand, Goldberg and Gasul,[7] in a series of 109 cases, reported the cutaneous test responsible for 37 per cent positive reactions, as compared with 39 per cent positive reactions with the Mantoux test.

The Mantoux modification is generally acknowledged to be the most sensitive of the tuberculin tests now in use, as borne out by many comparative studies. Objections raised against the Mantoux test are that the dilutions do not keep well, that the preparation of the solution and its technic require greater experience than the other tests, and that violent reactions may occur. There exists considerable controversy over the question of the stability of diluted tuberculin as employed in the Mantoux test. Maxwell [8] stated that the solution should be made up fresh every forty-eight hours. Others, including Myers [9] and Gaisford,[10] maintained that deterioration does not occur for two or three weeks afer dilution. Pilcher [11] and Ritter [12] stated that diluted tuberculin retains its potency indefinitely, for months and even years.

The applicability of the Mantoux test in varying dilutions constitutes an added advantage. Experience has shown that individuals who fail to react to the usual dosage of tuberculin may present a positive outcome when a more concentrated solution is employed. Blair and Galland [13] stated that positive reactions with dilutions of 1 : 100,000 or higher are considered indicative of active tuberculosis, whereas a response to a 1 : 10,000 dilution and not to any of the higher dilutions would connote latent or healed tuberculosis.

Goldberg and Gasul,[7] using the Moro test, obtained 20 per cent positive reactions, in contrast to 37 per cent with the Pirquet test. Rust,[14] with a modified Moro test—a concentrated tuberculin—reported

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6. Forbes, R., and Green, B.: Comparison of Value of Cutaneous and Intracutaneous Tuberculin Reactions, Arch. Pediat. **43**:736 (Nov.) 1926.

7. Goldberg, B., and Gasul, B.: The Dermatubin Test Compared with the von Pirquet, Moro and Mantoux Tuberculin Reactions, Illinois M. J. **57**:60 (July) 1930.

8. Maxwell, James: The Intradermal Tuberculin Test, Lancet **2**:1289 (Aug. 9) 1930.

9. Myers, J. A.: Tuberculosis Among Children, Menasha, Wis., The Collegiate Press, 1930.

10. Gaisford, Wilfrid F.: The Mantoux Test—An Analysis of 500 Cases, Lancet **1**:521 (March 7) 1931.

11. Pilcher, J. D.: Keeping Quality of Tuberculin Dilutions, J. A. M. A. **96**:1868 (May 30) 1931.

12. Ritter, John: Tuberculin Dilutions, J. A. M. A. **97**:480 (Aug. 15) 1931.

13. Blair, John E., and Galland, Walter I.: A Differential Quantitative Tuberculin Test, Am. Rev. Tuberc. **23**:1 (Jan.) 1931.

14. Rust, Byron K.: A Comparison of Tuberculin Skin Reactions, J. Indiana M. A. **33**:354 (Aug.) 1930.

96 per cent positive reactions, and with the Pirquet test only 76 per cent positive reactions. The same increased sensitivity to the modified Moro test, compared with the Pirquet test, was emphasized by Strachner, Wallgreen and Czikeli,[15] and Goldberg and Gasul,[7] the latter utilizing a mixture of killed tubercle bacilli in a concentrated glycerin tuberculin filtrate designated as tuberculin preparation.

Craig,[1] describing the "multiple puncture" test, emphasized the extremely slight traumatic tissue reaction. In a series of 283 cases, Forbes, Verploeg and Bazemore[16] obtained 36.14 per cent positive reactions with both the Mantoux and multiple puncture methods. This agreement in results was confirmed by Forbes and Steinberg[17] in a subsequent experience with 115 cases yielding 20 per cent postive results. Wahl and Gerstenberger[18] found the Mantoux test more markedly positive in 97 per cent of the cases.

It is evident from the foregoing brief review that, whereas the Mantoux test is generally regarded as the most reliable of the diagnostic tuberculin tests, each of the other modifications is in certain quarters considered equally dependable and, moreover, as possessing the advantage of greater simplicity of application.

It occurred to us that if the various modifications of the tuberculin test in common use were applied within a relatively short period in the same group of children, and the same preparation of tuberculin and a uniform technic were utilized, opportunity would thus be afforded for a more correct evaluation of these tests than is otherwise possible.

Accordingly, we performed 5 of the more commonly used tuberculin tests on the patients of the children's division of the National Jewish Hospital. The work was begun on Aug. 4, 1931, and completed eight weeks later. The group consisted of 55 children, 27 boys and 28 girls, from 4 to 17 years of age, with the majority from 6 to 13 years. A large proportion of the children had previously experienced intimate and protracted contact with persons having active tuberculosis. The majority were well nourished, ambulant and afebrile. The semiambulant and the bedfast comprised less than half the group. Nine children had open pulmonary tuberculosis of the adult type, and 8 tuberculosis of the bone or joints.

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15. Strachner, Wallgreen and Czikeli, in Rust, Byron K.: Comparison of Tuberculin Skin Reactions, J. Indiana M. A. **33**:354 (Aug.) 1930.

16. Forbes, R.; Verploeg, R., and Bazemore, M. K.: Survey of Tuberculosis in Schools in Colorado, Am. J. Dis. Child. **41**:26 (Jan.) 1931

17. Forbes, R., and Steinberg, C.: The Mantoux Versus the Craig Test, Am. J. Dis. Child. **40**:1230 (Dec.) 1930.

18. Wahl, S. A., and Gerstenberger, H. J.: A Statistical Study of Tuberculin Tests in Infancy, Arch. Pediat. **40**:143 (March) 1923.

TABLE 1.—*Results Obtained in Fifty-Five Children with Various Methods of Tuberculin Test*

| Test | Positive | Negative | Total | Per Cent Positive |
|---|---|---|---|---|
| Mantoux | 39 | 16 | 55 | 70.9 |
| Single puncture (intradermal) | 39 | 16 | 55 | 70.9 |
| Multiple puncture | 30 | 17 | 47 | 63.8 |
| Pirquet | 27 | 28 | 55 | 40.9 |
| Percutaneous | 16 | 31 | 47 | 34.0 |

TABLE 2.—*Size of Local Reaction According to Test Used*

| Test | Average Diameter, Mm. | Smallest Diameter, Mm. | Largest Diameter, Mm. |
|---|---|---|---|
| Mantoux | 11.6 | 6 | 21 |
| Single puncture | 7.9 | 3 | 15 |
| Multiple puncture | 7.9 | 4 | 12 |
| Pirquet | 6.3 | 3 | 11 |
| Percutaneous | ... | .. | .. |

TABLE 3.—*Number of Reactors, Grouped According to Size of Reaction*

| Test | Under 5 Mm. No Reactions | 5-9 Mm. | 10-14 Mm. | 15-19 Mm. | 20 Mm. and Over |
|---|---|---|---|---|---|
| Mantoux | 0 | 10 | 19 | 8 | 2 |
| Single puncture | 2 | 27 | 9 | 1 | 0 |
| Multiple puncture | 4 | 14 | 12 | 0 | 0 |
| Pirquet | 8 | 17 | 2 | 0 | 0 |
| Percutaneous | .. | .. | .. | .. | .. |

TABLE 4.—*Comparative Accuracy of the Five Tests*

| Reaction Negative with | Number Positive with: Mantoux | Single Puncture | Multiple Puncture | Pirquet | Percutaneous |
|---|---|---|---|---|---|
| Mantoux..... 16 (in 55 cases) | .. | 0 | 0 | 0 | 0 |
| Single puncture... 16 (in 55 cases) | 0 | .. | 0 | 0 | 0 |
| Multiple puncture 17 (in 47 cases) | 4 | 4 | .. | 3 | 2 |
| Pirquet..... 28 (in 55 cases) | 12 | 12 | 8 | .. | 4 |
| Percutaneous..... 31 (in 47 cases) | 18 | 18 | 14 | 7 | .. |

TABLE 5.—*Comparative Size of Reaction, According to Method Used*

| Reaction with | Equal to or Greater Than | Number of Instances |
|---|---|---|
| Single puncture | Mantoux | 2 |
| Pirquet | Mantoux | 1 |
| Multiple puncture | Mantoux | 4 |
| Pirquet | Single puncture | 9 |
| Pirquet | Multiple puncture | 4 |
| Single puncture | Multiple puncture | 14 |
| Multiple puncture | Single puncture | 19 |

The Mantoux, single puncture and Pirquet tests were performed on August 4, and the percutaneous and multiple puncture tests on October 10.

Mulford's human tuberculin was used, and a uniform technic was rigidly adhered to. The reactions were read by all co-workers. When agreement could not be reached, the opinion of the majority prevailed. Tests yielding equivocal results were repeated.

In the performance of the Mantoux test, 0.1 cc. of a 1 : 1000 dilution of old tuberculin, representing 0.1 mg., was used. In all negative cases the test was repeated with a dilution of 1 : 100. The Pirquet test was performed in the usual manner.

The "single puncture" method, thus far reported by only two observers, was performed by introducing a 22 gage needle into the dermal layer of the skin for a distance of 3/16 to 1/4 of an inch (0.48 to 0.64 cm.) through a drop of undiluted tuberculin previously deposited upon the forearm. The excess of tuberculin was removed, and no dressing applied. We estimated that by this means approximately 0.25 mg. tuberculin was delivered beneath the superficial layer of the skin.

In the performance of the percutaneous test we had anticipated using a tuberculin preparation for which results equal to those obtained with the Mantoux test are claimed, in preference to the less potent 50 per cent tuberculin ointment of Moro. We were unable to procure this product, and substituted old tuberculin Mulford, concentrated in vacuo to one-third its original volume by the research department of the hospital. A product of higher concentration could not be used because of extreme viscosity. It differs from the tuberculin preparation in that the latter is an emulsion of the tubercle bacillus, whereas our preparation consists of the products of their growth and possesses a potency about six times that of the Moro ointment. The site for this test was the manubrium sterni, previously cleansed with ether. The tuberculin was vigorously rubbed into the skin by means of the smooth end of a glass rod describing about 60 revolutions in an area not over 8 mm. in diameter. In a few patients, because of an acneform eruption, the forearm was substituted, with no apparent difference in results.

## EXPERIMENTAL WORK

*Method.*—The "multiple puncture" test is performed as follows. The tip of a large-sized sewing or darning needle held almost parallel to the surface of the skin is depressed with considerable pressure into a drop of tuberculin placed on the forearm; when the needle is raised, only the point is made to penetrate the superficial layer of the skin. This maneuver is repeated in rapid succession fourteen times—in contrast to six times, as recommended by Craig, which limits the field of operation to an area 4 or 5 mm. in diameter. Almost invariably slight oozing of blood occurred, which did not, however, influence the outcome.

It is our impression that the percutaneous modification caused the least discomfort to the children, and the Pirquet test the most.

The reactions were inspected at the end of twenty-four, forty-eight and seventy-two hours, and in a few instances at the expiration of four days. The reaction was most pronounced at the end of forty-eight hours. In a considerable number of patients, however, it was almost equally prominent at the end of twenty-four hours. Very few patients reached the height of their reaction at the expiration of twenty-four hours, with regression thereafter. Only occasionally was a reaction negative at the end of the first twenty-four hours and positive twenty-four hours later.

In no instance did we encounter any unfavorable local or constitutional effect, despite the inclusion in the group of a considerable number of patients with active tuberculosis.

The degree of reaction was estimated by the diameter of the resulting, sharply circumscribed red papule; the areola, when present, was disregarded. A nodule 5 mm. in diameter or larger was considered positive in connection with the Mantoux test, and one 3 mm. or larger with the Pirquet, "single puncture" and " multiple puncture" tests. The intensity of the percutaneous reaction was determined by the number of tiny, flat papules, frequently surmounted by vesicles.

*Reactions.*—The Mantoux test yielded 70.9 per cent positive reactions, the average papule having a diameter of 11.6 mm.; the smallest measured 6 mm., and the largest 21 mm. Over half the areas of reaction measured between 10 and 15 mm., and about a fifth between 15 and 20 mm. In no instance was a negative outcome witnessed with this method that the other methods did not likewise eventuate in a negative reaction. The intensity of the reaction was equaled or exceeded twice by the "single puncture" method, once by the Pirquet and four times by the "multiple puncture" method. The test was repeated in all negative cases, a 1 : 100 dilution being employed, with not a single reversal of the reaction.

The "single puncture" tests produced identically the same percentage of positive reactions as the Mantoux test. The average size attained by the papule was 7.9 mm., which is a trifle larger than that obtained with the Pirquet test and the same size as that obtained with the "multiple puncture" test. The largest area of reaction noted was 15 mm. in diameter. The largest number of children showed areas of reaction between 5 and 10 mm. in diameter. This test shares the distinction with the Mantoux test of not showing a single negative reaction that the other three tests did not likewise show. The areas of reactions produced by the Pirquet test in 9 children, and by "multiple puncture" in 16, equaled in size or were larger than those obtained with this modification.

The Pirquet test was positive in only 40.9 per cent of the cases, or in 30 per cent fewer than the two preceding tests. The average diameter of the papules was 6.3 mm.; the highest was 11 mm., with the majority yielding a papule between 5 and 10 mm. The test was negative in 12 children in whom a positive reaction was obtained by the Mantoux and "single puncture" methods, in 8 who gave positive reactions to the "multiple puncture" test and in 4 who gave positive reactions to the percutaneous test. The area of reaction in the Pirquet test frequently attained a considerable size, for in 9 of the patients it equaled or exceeded those resulting from the "single puncture" test, and in 4 patients it equaled or exceeded those obtained with the "multiple puncture" test.

The "multiple puncture" method ranks next to the Mantoux and "single puncture" methods in reliability, as evidenced by the percentage of positive reactions achieved, namely, 63.8 in 47 cases, demonstrating its unquestioned superiority over the Pirquet and the percutaneous tests. The average size of the area of reaction was identical with that resulting from the "single puncture" test, namely 7.9 mm., with 12 mm. as the largest diameter. Nearly half of the papules were between 5 and 10 mm. The outcome was negative four times when the Mantoux and "single puncture" tests were positive, three times when the Pirquet test was positive, and twice when the percutaneous test was positive. In 4 instances the reaction equaled or surpassed that of the Mantoux, and in 16 instances that of the "multiple puncture" test. In turn, the reaction obtained with the Pirquet and "single puncture" methods was, in 4 instances, as marked or even more pronounced than that from the "multiple puncture" test. In about 8 cases a slight reaction, in the form of a papule about 2 mm. in diameter, was encountered in children who gave negative reactions with the Mantoux and "single puncture" methods. These papules, by common consent, were considered traumatic.

Of all the tests, the percutaneous tests gave the smallest percentage of positive reactions, namely, 34 per cent in 47 children tested. The intensity of the reaction was determined by the number of papulo-vesiculopustules present, which varied from 2 to 10. On this basis, about one-third the number of positive reactions were designated moderate, and two-thirds as marked in degree.

## SUMMARY

Fifty-five children, chiefly of the preventorium type, with a generous admixture of active bone and pulmonary disturbances, ranging in age from 4 to 17 years and equally divided between the sexes, were subjected within a relatively short period to the application of the Mantoux, "single puncture," Pirquet, "multiple puncture" and percutaneous tests.

The Mantoux and "single puncture" modifications yielded the highest percentage of positive reactions—identical in both groups. We failed to

observe a single instance of a negative reaction from these tests that was not likewise negative with the other three modifications.

The lowest number of positive reactions, less than half of those obtained with the two previous tests, were obtained with the percutaneous method, and only a slightly higher percentage—namely, 7 per cent—with the Pirquet method.

The "multiple puncture" method resulted in 7 per cent fewer positive reactions than the Mantoux and "single puncture" methods. This test showed a considerable number of negative reactions in children who have positive reactions to the Pirquet and percutaneous modifications.

No unfavorable local or constitutional effects were encountered.

The most pronounced reactions were obtained with the Mantoux test. The papules from the "single puncture" method, however, though decidedly smaller in size, appeared equally distinctive.

## CONCLUSIONS AND RECOMMENDATIONS

A study of the various diagnostic tuberculin cutaneous tests, performed with scrupulous regard for details, demonstrated the utter unreliability of the Pirquet and the modified Moro tests.

It failed to substantiate the claims advanced by other observers for the "multiple puncture" method.

This study, in our opinion, demonstrated the superiority of the Mantoux and "single puncture" technic.

The recommendation appears warranted that these two tests supersede the others.

For routine office and bedside work the "single puncture method" may be given precedence, because it is easier to perform, is less time-consuming, eliminates the necessity for dilution and refrigeration, is less expensive and, withal, yields results as accurate as those obtained by the well established Mantoux test.

# EFFICIENCY OF NEW ORLEANS SUNSHINE IN PREVENTING RICKETS IN RATS

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That seasonal variation in the incidence of rickets is due to the changing amount of solar ultraviolet radiation shorter that 313 millimicrons is now universally accepted. Despite the decrease in the antirachitic solar radiation during the winter months, it has been shown that sunshine possesses a definite antirachitic effect throughout the year. Tisdall and Brown [1] in Toronto, Fleming [2] in Washington, D. C., and Wilder and Vack [3] in Boston found winter sunshine to be definitely antirachitic for rats even when passed through several of the substitutes for ordinary window glass. Caldwell and Dennett [4] in New York and Wyman and his collaborators [5] in Boston obtained similar results with infants. Similar studies have also demonstrated the seasonal variation in the ability of sunshine to prevent weakness of the legs in chickens.

The quality and intensity of the short ultraviolet radiations in sunlight are the determining factors in the prevention of rickets, and the correlation of the total number of hours of sunshine with the incidence of rickets in a particular locality and a comparison of such data with

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1. Tisdall, F. F., and Brown, A.: (*a*) Seasonal Variation of the Antirachitic Effect of Sunshine, Am. J. Dis. Child. **34**:721 (Nov.) 1927; (*b*) Antirachitic Value of the Sun's Rays Through Special Window Glasses, ibid., p. 742; (*c*) Relation of the Altitude of the Sun to Its Antirachitic Effect, J. A. M. A. **92**:860 (March 16) 1929; (*d*) Seasonal Variation in the Antirachitic Effect of Sunshine, Am. J. Dis. Child. **42**:1144 (Nov.) 1931.

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5. Wyman, E. T.; Drinker, P., and MacKenzie, K. H.: Antirachitic Value of Winter Sunlight in the Latitude of 42° 21′ (Boston), Am. J. Dis. Child. **39**: 969 (May) 1930.

those of other regions is of minor significance. Hess [6] pointed out that in the Panama Canal Zone, where rickets is practically nonexistent, not only is the yearly sunshine less than in New York but it is less evenly distributed.

New Orleans, a subtropical city, is of particular interest in this connection. Although the mean temperature of New Orleans is high, the weather bureau records show an average for the last forty years of only 58 per cent sunshine out of the total possible number of hours, an amount not greater than in many other cities in this country. Furthermore, being practically at sea level and having a humid climate (average relative humidity, 76 per cent), it might be expected that the antirachitic wavelengths would be absorbed and considerably diminished in their passage through the atmosphere. The relatively mild temperature, however, allows infants and children to be outdoors throughout most of the year. The availability of green vegetables, ample playing space and light clothing all tend to minimize the incidence of rickets. Severe rickets is rarely seen in New Orleans and its vicinity. Williams [7] studied the patients admitted to the Touro Infirmary in 1926 and reported that of 2,000 new admissions and 13,000 additional cases, only 1 patient showed malformation of the long bones. On the other hand, 45 per cent of 300 patients chosen at random had mild rickets. He found a correlation between the possible hours of sunshine and inorganic phosphorus, the later levels being in all cases higher than the figures given by Hess and Lundagen [8] in New York and the difference in phosphorus levels in winter and summer being less than 1 mg. per cent. Crawford and Williamson [9] also report a high incidence of mild rickets in New Orleans, and agree that severe rickets is rare, a conclusion supported by many of the local pediatricians. Mitchell [10] studied 500 white and 500 colored infants in Memphis, Tenn., during the spring months and found an incidence of 49.8 per cent of rickets in the white group and 87.6 per cent in the colored group; 11.2 per cent of the former and 34.6 per cent of the latter showed marked rickets.

In none of these local studies has an attempt been made to correlate the incidence and severity of rickets with the variations in the antirachitic wavelengths of sunlight, a factor which, in view of our present

6. Hess, A. F.: Ultraviolet Rays of the Sun, J. A. M. A. **84**:1033 (April 4) 1925.

7. Williams, C. T.: The Infrequency of Severe Rickets in New Orleans and Vicinity, Am. J. Dis. Child. **35**:590 (April) 1928.

8. Hess, A. F., and Lundagen, H. A.: Proc. Soc. Exper. Biol. & Med. **19**:380, 1922.

9. Crawford, R., and Williamson, G. R.: New Orleans M. & S. J. **83**:219, 1930.

10. Mitchell, F. T.: South. M. J. **23**:228, 1930.

knowledge, assumes the utmost importance. Our present study was therefore designed to measure physically and biologically the seasonal changes in the antirachitic efficiency of New Orleans sunshine and skyshine over a period of years.

Rats bred from our stock colony and weighing about 40 Gm. were divided into groups of 5 or 6 and fed the Steenbock 2965 rachitic diet, made up in quantities sufficient to last throughout the five or six weeks of an experiment. Distilled water was given ad libitum. The rats, housed in false bottom cages, so equipped that the contamination of food and water was reduced to a minimum, were kept together in a well ventilated, dimly illuminated room, the temperature of which was maintained fairly constant. Certain groups of animals were exposed to sunshine and skyshine on the roof of the animal house adjoining the laboratory. This building is situated on the college campus about 4 miles away from the business center at a latitude of 29° 56′ 2″ and about 35 feet above sea level. The atmosphere is reasonably clear of smoke and dust, although the animals were cut off from some of the radiation from the sky by high trees and buildings. The groups exposed to skyshine were placed on the same roof but in the shadow of the building and so received radiation from all directions except south. Certain animals were also exposed behind vitaglass, corex D and celoglass.[11]

The animals were usually exposed at 10 a. m., an hour appropriate for the exposure of infants in this climate. Exposures were given daily except in very cloudy weather or when it was raining. In clear weather an exposure of a certain length of time to sunshine means that direct sunshine and skyshine are exerting their effect; but when the sun is obscured, the rats receive skyshine only, that is, the diffusely reflected energy from the sky and clouds. Owing to the mildness of the climate, animals may be placed out of doors almost every day in winter with no provision for heating them. During the summer months the time of exposure was changed to 9:30 and 9:00 a. m. to avoid the debilitating effects of the excessive heat of the later part of the day.

The duration of almost all of the experiments was five weeks, which is usually sufficient for definite rickets to develop in control groups kept in the animal room, and in only a few instances was it necessary to continue the experiments longer. Each experiment included a control group in comparison with which the diagnosis was made for the most part on the basis of the line test and roentgenograms of the femurs and tibias. In some of the early experiments, determinations of serum phosphorus were also made.

11. The various screens were presented to us by the manufacturers, Vitaglass Corporation, Corning Glass Works and Acetol Products, Inc., respectively.

## TECHNIC

Special cages were used for exposing the animals behind the ultraviolet transmitting screens. The screens were cut to a standard size of 12 by 12 inches (30 by 30 cm.) and the cages so constructed that the screens could be quickly and easily removed for cleaning or replacement. The supporting pillars were made as narrow as possible to minimize shadows, and the solid back of the cage was always placed away from the sun, thus insuring a maximum exposure to the radiation. The glasses were kept as clean and free from dirt and grease as possible. The wavelength transmission of several pieces of each screen was measured before being exposed and at intervals during the course of the experiments by means of a Hilger ultraviolet and visible monochromatic illuminator and a Hilger visible and infra red spectrometer. Spectrograms of each piece of glass used were made with a large Hilger quartz spectrograph. The thirty-two pieces of vitaglass used in this study showed a short wavelength cut off somewhere between 253 and 281 millimicrons, depending on the thickness, which varied from 3 to 4 mm. Most of them cut off at about 260 millimicrons and showed an average transmission of from 30 to 33 per cent of the wavelengths between 290 and 303 millimicrons, and from 56 to 65 per cent of the wavelengths between 303 and 319 millimicrons. The thirty-eight pieces of corex D varied from 2 to 3 mm. in thickness and cut off quite uniformly at about 270 millimicrons. Four of the thicker pieces cut off at about 283 millimicrons, while two of the thinner pieces transmitted wavelengths down to 260 millimicrons. The transmission in the antirachitic region was about 40 per cent of the wavelengths between 290 and 303 millimicrons, and from 70 to 82 per cent between 303 and 319 millimicrons. The celoglass used in the construction of the cages was cut from a large roll. It showed a sharp cut off at 291 millimicrons and transmitted from 27 to 30 per cent of the wavelengths between 290 and 319. No effect of solarization could be detected in any of the screens even after 15 months of almost daily exposure, no doubt owing to the fact that the total time of exposure was relatively short.

The measurement of the solar and sky radiation was made on a tower built on the roof of the animal house adjacent to the place where the rats were being exposed. Such measurements were begun in 1928 and are still being continued. The extensive information we have thus obtained as to the variation in the total energy (intensity) and the distribution (quality) of sunshine and skyshine in New Orleans will be reported in detail elsewhere, only the pertinent data being referred to here. Spectrograms of the sun were made with a Zeiss spectrograph to determine the shortest wavelength present at the time of exposure. The intensity of the total energy of direct sunlight was determined by means of the pyrheliometer described by Gorczynski.[12] This consists of a large Moll surface thermopile and a registering millivoltmeter, the thermopile being carried on a clock-driven equatorial mounting, which, with a hand-operated altitude and azimuth adjustment, maintains the surface of the thermopile at right angles with the incident rays. The sun is accurately centered on the surface of the thermopile by means of a series of disks. The pyrheliometer is calibrated by exposure to a known amount of energy, and the amount of energy incident on the thermopile is expressed in gram calories per square centimeter of exposed surface. We have used a Leeds and Northrup galvanometer of high sensitivity in addition to the recording millivoltmeter. To obtain the distribution of the energy, screens with various cut-offs were used. The intensity of the antirachitic radiation was measured by interposing in front of the thermopile a piece of window glass with a transmission of 0.5 per

12. Gorczynski, L.: J. Optic. Soc. America **9**:455, 1924.

cent at 313 millimicrons, from 49 to 50 per cent at 334 millimicrons, 85 per cent at 365 millimicrons and about 90 per cent in the visible and near infra red. The long wave limit of the ultraviolet cut-off is taken at (and including) 313 millimicrons (instead of 310 millimicrons, the absolute cut-off), because it is a definite and easily obtained emission line (of the mercury arc spectrum) and, also, because antirachitic action terminates practically at this wavelength.

TABLE 1.—*Exposure to Sunshine and Skyshine*

| Experiment No. | Duration, 1929 | Daily Exposure, Min. | Total Time Sun + Sky Hr. | Sun + Sky Min. | Sky Hr. | Sky Min. | Average Daily Exposure Sun + Sky, Min. | Average Daily Exposure Sky, Min. | Average Energy Value Daily Exposure, Gm. Cal. per Sq. Cm. | Diagnosis |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | May 31-July 6 | 10 | 1 | 40 | 1 | 10 | 2.7 | 2.0 | 0.00119 | — |
| 2 | July 24-Aug. 29 | 20 | 5 | 35 | 9 | | 9.5 | 15.0 | 0.00548 | — |
| 3 | Sept. 26-Oct. 30 | 30 | 9 | 15 | 4 | 45 | 16.0 | 8.1 | 0.00614 | — |
| 4 | Oct. 8-Nov. 12 | 10 | 3 | 5 | 1 | 50 | 5.1 | 3.0 | 0.00270 | — |
| 5 | Oct. 30-Dec. 4 | 30 | 7 | | 5 | | 11.7 | 8.3 | 0.00423 | — |
| 6a | Nov. 16-Dec. 20 | 10 | 3 | 10 | 1 | | 5.4 | 1.7 | 0.00179 | — |
| 6b | Nov. 16-Dec. 20 | 20 | 6 | 20 | 2 | | 10.8 | 3.4 | 0.00358 | — |
| 7 | Dec. 5-Jan. 17 | 30 | 8 | | 6 | | 14.0 | 10.0 | 0.00195 | — |
| | 1930 | | | | | | | | | |
| 8 | Jan. 3-Feb. 14 | 10 | 3 | 10 | 1 | 40 | 4.5 | 2.4 | 0.00102 | — |
| 9 | Feb. 10-Mar. 24 | 10 | 2 | 20 | 1 | 20 | 3.3 | 1.9 | 0.00071 | 4 —; 2 ++ |
| 10 | Feb. 24-Mar. 31 | 5 | | 45 | | 30 | 1.3 | 0.8 | 0.00045 | 3 +++; 3 ++++ |
| 12 | Mar. 29-May 1 | 10 | 3 | | 1 | 20 | 5.5 | 2.4 | 0.00290 | — |
| 14 | May 3-June 7 | 5 | 1 | 15 | | 50 | 2.2 | 1.4 | 0.00167 | — |
| 15 | May 17-June 24 | 5 | 1 | 45 | | 30 | 2.7 | 0.8 | 0.00158 | — |
| 17a | June 16-July 21 | 5 | 2 | 10 | | 20 | 3.7 | 0.6 | 0.00217 | — |
| 17b | June 16-July 21 | 5* | 1 | | | 15 | 1.7 | 0.1 | 0.00099 | 3 —; 2 ++ |
| 19a | July 25-Sept. 4 | 8 | 1 | 20 | 2 | 16 | 1.9 | 3.3 | 0.00086 | — |
| 19b | July 25-Sept. 4 | 10 | 1 | | 1 | 40 | 1.4 | 2.4 | 0.00064 | — |
| 20 | Sept. 5-Oct. 10 | 5 | 1 | 5 | 1 | 20 | 1.9 | 2.1 | 0.00052 | — |
| 21 | Nov. 24-Dec. 29 | 20 | 3 | 20 | 4 | | 5.4 | 6.7 | 0.00175 | — |
| | 1931 | | | | | | | | | |
| 22 | Jan. 5-Feb. 9 | 10 | 2 | 30 | 1 | | 4.3 | 1.7 | 0.00086 | 2 ++; 2 +++ |
| 23 | Feb. 19-Mar. 26 | 15 | 4 | 40 | 1 | 30 | 8.0 | 2.7 | 0.00308 | — |
| 24 | April 7-May 12 | 5 | 1 | 20 | 1 | | 2.3 | 1.7 | 0.00096 | — |
| 26 | May 16-June 20 | 5 | 1 | 30 | | 50 | 2.6 | 1.4 | 0.00115 | — |
| 27 | June 5-July 11 | 5 | 1 | 5 | 1 | 20 | 1.8 | 2.2 | 0.00061 | — |
| 28 | June 24-July 29 | 5 | | 55 | 1 | 10 | 1.6 | 2.0 | 0.00054 | — |
| 29a | July 17-Aug. 20 | 5* | 1 | | | 15 | 1.7 | 0.4 | ..... | — |
| 29b | July 17-Aug. 20 | 5† | | 40 | | 15 | 1.1 | 0.4 | ..... | — |
| 30 | July 31-Sept. 1 | 5 | | 50 | 1 | 15 | 1.6 | 2.3 | ..... | — |
| 31a | Aug. 24-Sept. 26 | 5 | 1 | 10 | 1 | 10 | 2.1 | 2.1 | ..... | — |
| 31b | Aug. 24-Sept. 26 | 5‡ | | 30 | | | 0.9 | 0.0 | ..... | — |
| 32 | Sept. 30-Nov. 4 | 5 | 1 | 25 | | 50 | 2.4 | 1.4 | 0.00090 | 2 —; 3 ++ |
| 33 | Nov. 21-Dec. 26 | 8 | 1 | 44 | | 24 | 2.7 | 0.7 | ..... | 1 —; 5 + |

In the third column * indicates three times each week; †, twice a week; ‡, on clear days only; in the last column, — indicates no rickets; +, borderline; ++, mild; +++, moderate, and ++++, florid rickets.

## EXPOSURE TO SUNSHINE

An arbitrary exposure of ten minutes was chosen for the first experiment, which began on May 31 and ended on July 6, 1929. Since then a total of 33 experiments has been made, the results of which are shown in table 1. As previously mentioned, when animals are exposed to sunshine they also receive a large amount of radiant energy from the hemispheric dome of the sky; when it is cloudy the ratio of this skyshine to direct sunshine is high. We have indicated the total and average times of exposure to sunshine (sun plus sky, columns 4 and

6) and to skyshine alone, that is to say, when the sun was obscured by clouds (sky, columns 5 and 7). During particularly cloudy months, the rats actually received more skyshine than sunshine, as in experiments 2, 19, 20, 21, 27, 28 and 30. The discrepancies in the sums of the average values (columns 6 and 7) and the daily exposures (column 3) are due to the variation in the number of rainy or cloudy days.

A daily exposure of from 10 to 30 minutes (with an average of from 2.7 to 14 minutes) to sunshine and skyshine was more than adequately protective in the first 8 experiments, extending from May 31, 1929, through Feb. 14, 1930. Since our chief aim was to determine the seasonal variation in the minimum amount of antirachitic radiation in New Orleans sunlight, we accordingly shortened the exposures in the succeeding experiments. The minimum time of exposure was set at 5 minutes, and in some cases this period was obviously longer than necessary. To secure further information on this point, a few groups of rats, while exposed for 5 minutes, were put out only 2 or 3 times a week. An average daily exposure to sunshine (and skyshine) of between 2 and 3 minutes was amply antirachitic from April through October. Of particular interest are experiments 1, 15 and 26 during similar periods (May and June) of 1929, 1930 and 1931, in which protection was afforded by average daily exposures of 2.7, 2.7 and 2.6 minutes, respectively. The minimum effective exposure from November through March was found to be from 5 to 6 minutes, shorter exposures during this period (experiments 9, 10, 22 and 33) being only partially protective. We have included experiments 9, 10 and 23, performed during the latter half of February and March, in this grouping, although the minimum effective time used was 8 minutes (experiment 23). Since 3.3 minutes (experiment 9), however, was almost completely protective, we have taken the mean value as representing the approximate threshold. Note should be made that although an average daily exposure of 1.3 minutes during the latter part of February and March (experiment 10) was followed by severe rickets, an average daily duration of 1.4 minutes was protective from July 25 to September 4 (experiment 19b).

Vitaglass was first used in experiment 7 and in 15 subsequent experiments, corex D in 8 and celoglass in 7. Animals exposed to sunlight through these screens, as contrasted to the adequate duration without them, require longer exposures, depending on the amount of antirachitic radiation that the screens transmit. For example, with vitaglass an effective exposure would have to be at least 2 to 2.5 times as long as to direct sunlight. The calculated effective exposures through vitaglass are from 4 to 7.5 minutes from April through October and from 10 to 15 minutes from November through March; for corex D,

they are about from 3 to 4 minutes and 6 to 8 minutes, and for celoglass, from 7 to 10 and from 17 to 20 minutes, respectively. Our actual findings are in general agreement with these calculated values, which indicates that our average exposures to direct sunshine (without the screens) were fairly close to the minimum duration necessary for the prevention of rickets.

During the winter months there is little radiant energy shorter than 313 millimicrons in New Orleans sunlight, except on brilliantly clear days. The average values for the months of the year and the number of determinations from which they were derived are given in table 2. These averages were obtained from measurements made only on clear days or when the sun was not obscured by clouds. Since there are more cloudy and rainy days than there are clear days in New Orleans (average for 60 years shows only 124 clear days), the values

TABLE 2.—*Average Amounts of Antirachitic Radiation During the Year at 10 A. M.*

| Date | No. of Days Measured, 1930 | Gm. Calories per Sq. Cm. per Minute | Microwatts per Sq. Cm. | No. of Days Measured, 1931 | Gm. Calories per Sq. Cm. per Minute | Microwatts per Sq. Cm. |
|---|---|---|---|---|---|---|
| January | 3 | 0.000252 | 17.64 | 6 | 0.000226 | 15.82 |
| February | 5 | 0.000213 | 14.91 | 5 | 0.000195 | 13.65 |
| March | 5 | 0.000385 | 26.96 | 5 | 0.000401 | 28.07 |
| April | 6 | 0.000528 | 36.96 | 3 | 0.000485 | 33.95 |
| May | 9 | 0.000563 | 39.41 | 4 | 0.000453 | 31.71 |
| June | 4 | 0.000836 | 58.52 | 4 | 0.000565 | 39.55 |
| July | .. | ..... | ..... | 2 | 0.000634 | 44.38 |
| August | 3 | 0.000572 | 40.04 | 1 | 0.000737 | 51.59 |
| September | 3 | 0.000452 | 31.64 | .. | ..... | ..... |
| October | 7 | 0.000373 | 26.11 | 4 | 0.000374 | 26.18 |
| November | 6 | 0.000278 | 19.46 | 3 | 0.000274 | 19.18 |
| December | 5 | 0.000183 | 12.81 | .. | ..... | ..... |

given represent the approximate upper limits that may be expected. Coblentz, Stair and Hogue [13] obtained values ranging from 60 to 80 microwatts at 10 a. m. during June in Washington and about 57 in July. After a careful study, they conclude that the average amount of ultraviolet radiation of wavelengths less than, and including, 313 millimicrons for midlatitude sea level stations, during the clearest weather, during midday in summer, amounts to about 0.00129 Gm. calory per square centimeter per minute (90 microwatts per square centimeter) decreasing to about 0.000285 Gm. calory per square centimeter per minute (20 microwatts per square centimeter) on the clearest days in midwinter. Our values for midsummer midday are of the same order, ranging from 65 to 70 microwatts, although we sometimes obtained values of from 38 to 49 microwatts on clear days in midwinter. The weather for the year 1930 was considered by the local weather bureau as being remarkably near the normal, or long term mean, and

13. Coblentz, W. W.; Stair, R., and Hogue, J. M.: Bur. Stand. J. Research **7**:723, 1931.

the total number of determinations represent over one third of the clear days during the year. The differences in the values for similar months in 1930 and 1931 reflect the variations in the amount of haze and clouds present at the time. The single value for August, 1931, was obtained on an unusually clear, dry day. A greater number of readings would probably have shown a smaller average value for the month, as was the case in 1930, since the weather in New Orleans during July and August is usually cloudy, the average number of clear days for the last 56 years being only 7 and 8, respectively, as compared with 10 in December and 16 in October. DeBuys [14] and DeBuys and von Meysenbug [15] found that the peak of incidence of rickets in infants in New Orleans varied in different years. Thus, in 1922, they found the greatest incidence during March, while in the following year, the peak had shifted to late in July. Our findings for 1930 and 1931 stress the explanation of this variation in time of incidence as being the variation in the amount of antirachitic radiation.

Spectrograms were taken several times during the day on clear days, always while the animals were being exposed. At this time of the day, the spectrum rarely extends to 300 millimicrons, and we have only one record, that for June 6, 1930, of 299 millimicrons. During the winter months the spectrum rarely extends below 306 millimicrons except on clear days following a rain storm, when the air has been washed clear. In fact, throughout the year relatively few days are found in which the spectrum, even at noon, extends below 304 millimicrons. From June 1 to Dec. 31, 1929, only 5 of 55 days measured showed limits lower than 304 millimicrons, only 7 days of 77 in 1930, and only 15 days of 50 in 1931. Air pollution, clouds and haze shorten the extent of the spectrum so that even in August, for days on end, there are no wavelengths shorter than 310 millimicrons. In many cases, there must be considerable carry-over of antirachitic effect from those days when the shorter wavelengths are present (Russell and Howard [16]). In experiment 31b, six 5 minute exposures on clear days over a period of 5 weeks protected a group of rats as adequately as did a 5 minute daily exposure of another group for the same length of time. Since solar radiation of the most effective antirachitic wavelengths, 302 millimicrons and shorter, is so seldom present in this city, and since it is possible at all times of the year to prevent rickets in rats by exposing them to the

14. DeBuys, L. R.: Clinical Study of Rickets in the Breast-Fed Infant, Am. J. Dis. Child. **27**:149 (Feb.) 1924.

15. DeBuys, L. R., and von Meysenbug, L.: Effect of Routine Administration of Cod Liver Oil on Development of Rickets in the Breast Fed, Am. J. Dis. Child. **28**:329 (Sept.) 1924.

16. Russell, W. C., and Howard, C. H.: J. Biol. Chem. **91**:493, 1931.

available sunshine, the conclusion is obvious that the effects are being exerted, for the most part, by wavelengths between 304 and 313 millimicrons.

The smallest amount of solar energy of wavelengths less than 313 millimicrons that was protective in our experiments (table 1) was an average of 0.00052 Gm. calory per square centimeter daily (experiment 20), amounting to a total of 0.0182 Gm. calory per square centimeter. The usual wavelength cut-off during this period was 304 millimicrons or above, the spectrum extending to 301 millimicrons on one of the days measured. Our results show that an average daily exposure to less than about 0.001 Gm. calory per square centimeter of wavelengths less than 313 millimicrons was partially or completely antirachitic from April through October, while exposures of 0.001 to 0.002 Gm. calory per square centimeter were effective during the remainder of the year.

The effective exposures to sunshine that we used are shorter than any concerning which reports have been published. Day [17] has reported from Little Rock, Ark., that the average daily amount of sunshine necessary to afford the same partial protection against rickets in rats receiving a rachitogenic diet varied from 5 minutes in May, June and July to 168 minutes in December, with intermediate values for the other months. Stein and Lewis [18] published results on the exposure of rats to sunshine in Denver during June and July, 1927. They found an average daily exposure of 1.957 minutes inadequate, some protection with 3.75 minutes and more or less complete protection with exposures greater than 7.5 minutes. They conclude that their results indicate that the effective biologic rays of sunlight are quantitatively of a greater magnitude in Colorado than in other places studied and ascribe this to the comparative freedom of the atmosphere from moisture and dust. They report, as did Forbes, Green and Stephenson,[19] a low incidence (from 24 to 29.5 per cent) of rickets in children in Colorado. Lewis, Frumess and Stein [20] do not find a seasonal variation in antirachitic efficiency in Denver, where, throughout the year the antirachitic wavelengths reach the earth, owing to the high percentage of sunshine, the low humidity and the small amount of smoke in the atmosphere.

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17. Day, P. L.: Seasonal Variation in Antirachitic Action of Arkansas Sunshine, Am. J. Dis. Child. **43**:1455 (June) 1932.

18. Stein, H. B., and Lewis, R. C.: Rickets, Am. J. Dis. Child. **41**:62 (Jan.) 1931.

19. Forbes, R. P.; Green, B., and Stephenson, F. B.: Arch. Pediat. **43**:131, 1926.

20. Lewis, R. C.; Frumess, G. M., and Stein, H. B.: Comparison of Antirachitic Effects of Winter and Summer Sunshine in Colorado, Am. J. Dis. Child. **41**:71 (Jan.) 1931.

Godfrey [21] has also reported the lack of seasonal variation in solar antirachitic efficiency in Honolulu.

The relatively high intensity of the available radiation in New Orleans throughout the year accounts for the short exposures necessary to prevent rickets. Another important factor has been pointed out by Tisdall and Brown.[22] There is a marked increase in the antirachitic effect of sunshine in Toronto when the sun reaches a midday altitude of 35 degrees, late in February, and a marked decrease at about the same altitude in October. The increased antirachitic effect with the sun at 35 degrees is due to a general increase in the intensity of the rays ranging from 320 to 294 millimicrons rather than to the presence of shorter rays that do not get through with the sun at the lower altitudes. Dick [23] showed that severe rickets was rare, or absent, in all places where the minimal seasonal altitude of the sun was about 35 degrees, and Tisdall and Brown believe that severe rickets occurs in those places where the altitude of the sun is below 35 degrees for several months of the year. They think [1d] that the failure of Lewis, Frumess and Stein to find any seasonal variation in solar antirachitic radiation is probably due to the fact that their experiments were made in February, March and April, at which time the sun in Denver had already reached an altitude of 35 degrees and therefore had a high antirachitic potency. Taking into account the latitude and altitude (1650 meters) of Denver, Tisdall and Brown would expect to find in that city a low antirachitic effect of sunshine only from December 1 to January 15. Since the minimal seasonal midday altitude of the sun in New Orleans is 37 degrees, one would presume that severe rickets would be comparatively rare. Although we were able to prevent the appearance of rickets throughout the year, there is a suggestion that the difference in the sun's altitude at the time of exposure may account in some measure for the seasonal variation that we observed at this hour. The altitude of the sun at 10 a. m. is 32, 29 and 32 degrees during November, December and January, respectively, and is above 35 degrees in February and October. Our results show that the effective exposure is longer during November, December and January, with an increase in effectiveness in the latter part of February.

## EXPOSURE TO SKYSHINE

The importance of skyshine as a source of ultraviolet radiation was first pointed out by Dorno.[24] He showed that at Davos (altitude, 1560

21. Godfrey, L. S.: J. Prev. Med. **5**:1, 1931.

22. Tisdall and Brown (footnote 1 *c* and *d*).

23. Dick, J. L.: Rickets, New York, E. B. Treat & Company, 1922.

24. Dorno, C.: Physik der Sonnen und Himmelsstrahlung, Braunschweig, Friedr. Vieweg u. Sohn, 1919.

meters), even under the best conditions and with a solar altitude of 60 degrees, the ultraviolet radiation of wavelengths less than 366 millimicrons in direct sunshine was only 90 per cent of that in skyshine. With lower solar altitudes the ultraviolet radiation in skyshine increases markedly, so that with a solar altitude of 30 degrees, sunshine contains only about 30 per cent as much ultraviolet as skyshine. In going from Davos to Muottas-Muraigl (altitude 2450 meters), Dorno [25] found that the total ultraviolet radiation of the sky decreases about 10 per cent, while the direct solar ultraviolet radiation increases 66 per cent. Pettit [26] also showed that about 50 per cent of the total amount of ultraviolet rays observed at an elevation of 257 meters was contributed by the sky, while at an elevation of 1737 meters, it contributed only about 30 per cent of the total amount of ultraviolet rays measured. On the other hand, the total ultraviolet radiation (sun and sky) observed at the high elevation was only 5 per cent greater than at the lower elevation. Clark [27] reported that the antirachitic energy (from 290 to 315 millimicrons) in north sky in Baltimore during the winter months was as intense as that in direct sunshine, and that in the summer months the intensity of direct solar antirachitic radiation was about 3 times that of north sky. Our own measurements during the month of July, 1931, show that in New Orleans, with a solar altitude of about 61 degrees, the intensity of the ultraviolet of wavelengths less than 313 millimicrons is about 20 per cent greater in skyshine than in direct sunshine.

Tisdall and Brown adequately described the terms sunshine and skyshine: The term skyshine is used to designate the sun's rays that are reflected from the sky and clouds, in contradistinction to the rays received from the sun itself. For example, an object placed on the sunny side of the street receives not only the rays from the sun but also the reflected rays from the sky. If an object is placed on the shady side of the street, only the rays reflected from the sky (skyshine) are received. If the object is again placed on the sunny side of the street and if a long cylinder pointed directly at the sun is placed over the object, the rays from the sky are cut off by the walls of the cylinder and only the rays directly from the sun pass along the inside of the cylinder to the object at the bottom. It is obvious that animals or infants exposed to sunshine also receive skyshine. Tisdall and Brown [28] demonstrated that December skyshine in Toronto has an antirachitic effect almost as marked as that obtained by exposure to the then availa-

25. Dorno, C.: Grundzüge des Klimas von Muottas-Muraigl, Braunschweig, Friedr. Vieweg u. Sohn, 1927.

26. Pettit, E., quoted from Coblentz, W. W., and Stair, R.: Bur. Stand. J. Research **6**:951, 1931.

27. Clark, J. H.: J. Optic. Soc. America **4**:240, 1931.

28. Tisdall, F. F., and Brown, A.: Antirachitic Effect of Skyshine, Am. J. Dis. Child. **34**:737 (Nov.) 1927.

ble sun, and that in general, skyshine had from one-half to two-thirds as great a potency in preventing rickets in rats as had sunshine, that is, sunshine and skyshine. Fleming [29] also found skyshine in Washington to be effective in preventing rickets in rats. The greater uniformity in the ultraviolet content of skyshine has been pointed out by Godfrey,[21] Clark,[27] Earp [30] and others and is suggestive that skyshine may perhaps be a more effective therapeutic agent than is sunshine.

TABLE 3.—*Exposure to Skyshine*

| Experiment No. | Duration of Experiment, 1929 | Daily Exposure, Minutes | Total Time Hr. | Total Time Min. | Average Daily Exposure, Minutes | Diagnosis |
|---|---|---|---|---|---|---|
| 1 | May 31–July 6 | 10 | 4 | 50 | 8.3 | ++ |
| 2a | June 24–July 29 | 30 | 14 | 5 | 24.0 | — |
| 2b | June 24–July 29 | 60 | 28 | 10 | 48.0 | — |
| 3 | Sept. 26–Oct. 30 | 180 | 81 | 35 | 140.0 | — |
| 4 | Oct. 8–Nov. 12 | 30 | 14 | 20 | 24.0 | — |
| 5 | Oct. 30–Dec. 4 | 180 | 72 | | 120.0 | — |
| 6a | Nov. 16–Dec. 20 | 30 | 13 | | 22.0 | — |
| 6b | Nov. 16–Dec. 20 | 90 | 36 | 30 | 63.0 | — |
| 7 | Dec. 5–Jan. 17 | 180 | 84 | | 148.0 | — |
| | 1930 | | | | | |
| 8 | Jan. 3–Feb. 14 | 90 | 47 | 50 | 67.0 | — |
| 9 | Feb. 10–Mar. 24 | 60 | 20 | | 28.0 | 4 —; 2 + |
| 10 | Feb. 24–Mar. 31 | 30 | 8 | 30 | 15.0 | ++++ |
| 12 | Mar. 29–May 1 | 60 | 26 | | 47.0 | — |
| 14 | May 3–June 7 | 30 | 12 | 30 | 22.0 | — |
| 15 | May 17–June 24 | 20 | 9 | | 14.0 | 1 —; 2 ++; 2 +++ |
| 17 | June 16–July 21 | 20 | 9 | 40 | 16.0 | 1 —; 2 ++; 2 +++ |
| 19 | July 25–Sept. 4 | 20 | 9 | 20 | 13.6 | ++ |
| 21 | Nov. 24–Dec. 30 | 60 | 23 | | 35.0 | — |
| | 1931 | | | | | |
| 22 | Jan. 5–Feb. 9 | 60 | 26 | | 44.6 | — |
| 23 | Feb. 19–Mar. 26 | 45 | 11 | | 16.0 | — |
| 24 | April 7–May 12 | 30 | 14 | 30 | 25.0 | — |
| 26 | May 16–June 20 | 20 | 9 | 20 | 16.0 | — |
| 27 | June 5–July 11 | 15 | 7 | 15 | 11.8 | — |
| 28 | June 24–July 29 | 20 | 9 | | 15.3 | — |
| 29 | July 17–Aug. 20 | 15 | 7 | 15 | 12.4 | — |
| 30 | July 31–Sept. 1 | 20 | 8 | 20 | 15.5 | — |
| 31 | Aug. 24–Sept. 26 | 20 | 9 | 20 | 16.5 | — |
| 32 | Sept. 30–Nov. 4 | 20 | 9 | | 15.4 | 3 ++; 2 +++ |
| 33 | Nov. 21–Dec. 26 | 30 | 8 | | 13.3 | 3 +; 2 ++; 1 +++ |

Our first arbitrarily chosen exposure of 10 minutes daily to skyshine (average daily exposure of 8.3 minutes from May 31 to July 6, 1929, experiment 1) resulted in moderate rickets in all of the animals. The duration of the exposures was accordingly considerably increased in the succeeding experiments. The data are given in table 3. An average daily exposure to skyshine of from 16 to 17 minutes is close to the minimum effective amount which will prevent rickets in rats in New Orleans from May through September, although somewhat shorter

29. Fleming, W. D.: Mil. Surgeon **63**:658, 1928.

30. Earp, J. R.: Am. J. Hyg. **12**:696, 1930.

exposures during June, July and August, 1931, were protective. Thus the antirachitic action of skyshine is at least one-sixth as potent as that of sunshine (and skyshine) during these months.

Average daily exposures to skyshine of from 22 to 24 minutes (about four times those of sunshine plus skyshine) were adequate during October, November and December. The exposures of 67 and 44.6 minutes used in January (experiments 8 and 22) were unquestionably too long. Judging from the average exposures found adequate in December and February, an average daily exposure of from 22 to 28 minutes would have been effective. The results for February and March, 1930, and 1931 vary. Thus an average daily exposure of 28 minutes from Feb. 10 to March 24, 1930 (experiment 9), was not quite sufficient, although an average daily exposure of 16 minutes from Feb. 19 to March 26, 1931 (experiment 23), was protective. Similar durations of exposure (15 and 16 minutes) during March of 1930 and 1931 (experiments 10 and 23) resulted in florid rickets in the former, and no rickets in the latter case. The effective exposures of 47 minutes (experiment 12) and 25 minutes (experiment 24) during April were probably longer than necessary. We may conclude that an average daily exposure of less than 28 minutes would be effective in February, and that exposures of from 16 to 20 minutes are protective in March and April.

Partial or complete protection was afforded to rats exposed daily to skyshine under vitaglass from May through September for average periods of from 28.8 to 50 minutes. This was to have been expected from the transmission data of this screen. Similarly, from October through January average daily exposures of 51.1 to 67 minutes were antirachitic. The results for February, March and April for 1930 and 1931 differ, as did the results on direct skyshine, although the results with and without the screen are consistent for each year. Exposures of 28.3 to 50 minutes were adequate in 1931, but not so in 1930. This would indicate that the differences obtained were due to variations in the amounts of antirachitic radiation present at these times in the two years.

Animals exposed to skyshine under corex D from June through September obtained almost complete protection with average daily exposures of from 23 to 28 minutes, and average exposures of 40 to 50 minutes were protective from January through April. The results with celoglass show that sufficient protection was afforded during June and July with average daily exposures of from 23 to 48 minutes, but that relatively long exposures (up to 94 minutes) were inadequate at other times of the year. Our results do not prove that this screen

is entirely ineffective, except during the summer months, but they do indicate that for exposure to skyshine, screens with better transmission in the antirachitic region would be more desirable.

During the months of June and July, 1931, measurements of skyshine, as well as sunshine and skyshine, were made with the Epply pyrheliometer, a modification of that designed by Kimball and Hobbs.[31] This instrument differs from the Gorczynski pyrheliometer in that the radiation is measured on a horizontal plane and includes skyshine as well as sunshine. This instrument thus receives the total radiation to which the animals were exposed. By shielding the thermopile from the direct solar rays it is possible to measure skyshine, and thus determine the part it plays in making up the total radiation. Thus the average total energy of wavelengths less than 313 millimicrons (sunshine and skyshine) during experiment 27 was 0.000407 Gm. calory per square centimeter per minute which, multiplied by the duration of the exposure to sunshine (1.8 min., table 1), gives 0.00073 Gm. calory per square centimeter as the average total antirachitic energy of a single exposure. In addition (table 1) the animals received an average of 2.2 minutes of skyshine daily. The average total radiation of less than 313 millimicrons in skyshine for this period was 0.000290 Gm. calory per square centimeter per minute. The sum of these values, the total amount of antirachitic radiation that the rats received, was 0.00137 Gm. calory per square centimeter daily. The skyshine group in this series received an average daily exposure of 11.8 minutes (table 3), which is equivalent to 0.0034 Gm. calory per square centimeter of wavelengths less than 313 millimicrons. Similar treatment of the data for experiment 28 shows that the animals in the sunshine group received a total of 0.0012 Gm. calory per square centimeter daily of wavelengths less than 313 millimicrons as compared to the skyshine group which received 0.0037 Gm. calory per square centimeter daily. Correlation of the physical data with the biologic findings indicates that much shorter exposures to skyshine during this period would still have been effective.

Our experiments justify the conclusion that there is ample antirachitic radiation present in sunshine (sunshine and skyshine) and in skyshine to prevent rickets throughout the year in New Orleans, and that this radiation is adequate to provide protection even when passed through the ordinary window glass substitutes which are in common use.

## SUMMARY

Exposure of rats on a rachitogenic diet (Steenbock 2965) over a period of 31 months shows that an average daily exposure to New

31. Kimball, H. H., and Hobbs, H. E.: J. Optic. Soc. America **7**:707, 1923.

Orleans sunshine (sun plus sky) of from 2 to 3 minutes from April through October prevents the appearance of rickets, as do average daily exposures of from 5 to 6 minutes from November through March. Vitaglass, corex D and celoglass were found to transmit ample solar antirachitic radiation throughout the year to prevent the appearance of rickets.

Average daily exposures to skyshine of from 16 to 17 minutes from May through September prevent rickets, as do average daily exposures of from 22 to 28 minutes from October through February, and from 16 to 20 minutes during March and April. Rats exposed to skyshine under vitaglass and corex D are protected throughout the year by correspondingly longer exposures. Celoglass was relatively ineffective except during the summer months.

The average daily amount of direct solar radiation of wavelengths shorter that 313 millimicrons which will prevent rickets is equivalent to less than 0.001 Gm. calory per square centimeter (70 microwatts) from April to October, and between 0.001 and 0.002 Gm. calory per square centimeter during the rest of the year. Measurement of the total antirachitic radiation, which includes the additional skyshine to which the animals are exposed, shows that in June and July antirachitic radiation from sunshine and skyshine equivalent to between 0.0012 Gm. calory (84 microwatts) and 0.0014 calory (98 microwatts) per square centimeter daily will prevent rickets in rats.

# EFFECT OF SUNSHINE THROUGH WINDOW GLASS AND FRESH AIR ON RESISTANCE TO INFECTION

## EXPERIMENTS ON ANIMALS

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In the following experiments it is shown that the exposure of rachitic rats to sunshine transmitted by common window glass outdoors markedly raises their resistance to an oral infection with "rat typhoid," although the rickets is not improved. The beneficial effect of exposure to fresh air alone is approximately half that of the combination of fresh air and sunshine through glass. The addition of vitamin D to this rachitogenic diet also increases the resistance of the rats to the infection, and if they are exposed to sunshine under window glass as well, the resistance is still further raised.

### SOLAR RADIATION

The radiation from the sun that reaches the earth possesses wavelengths that vary from 290 to 4,000 millimicrons [1] (mμ), or from 2,900 to 40,000 angstrom units. These radiations are electromagnetic and comprise but a small portion of the entire known range of wavelengths, which vary all the way from the extremely short cosmic rays to the very long waves used in wireless telegraphy. Solar radiation may be divided into three regions: ultraviolet, visible and infra-red. The wavelengths of the ultraviolet radiation are between 290 and 380 mμ. Then follow the wavelengths (from 380 to 760 mμ) that produce visible light, and these are only a small portion of the solar radiation. Beyond the red end of the visible spectrum are the infra-red rays with wavelengths from about 760 to 4,000 mμ. The red and near infra-red radiations in the wave band from 650 to 1,400 mμ are able to penetrate some distance below the skin before they are completely absorbed, and

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1. A millimicron is one millionth of a millimeter in length.

thus produce deep heating effects. The longer infra-red rays are less penetrating.[2]

*Ultraviolet Rays.*—Numerous investigations have been carried out in recent years to determine the effect of exposure not only of the animal organism, but also of foods and oils to short ultraviolet rays. It has been found that a narrow band in the solar ultraviolet extending from 290 to 302 mμ (or possibly to 310) cures or prevents rickets,[3] and that the administration of food that has been exposed to ultraviolet rays has a similar beneficial effect.[4] It has also been shown that the erythema-producing waves from the sun correspond closely with the antirachitic zone,[5] although not exactly, as skyshine has an antirachitic effect but produces no pigmentation.[6] Common window glass does not transmit any of the ultraviolet that is curative for rickets, as it is opaque to wavelengths shorter than about 310 mμ.

As to the therapeutic value of irradiation with an artificial source of ultraviolet rays in other clinical conditions, there is considerable difference of opinion. The effect of irradiation with a mercury vapor lamp on the incidence of colds in volunteers of various ages was studied by Maughan and Smiley.[7] They found that there was an apparent reduction in the number of colds of from 40 to 55 per cent, but the controls in these experiments were not entirely satisfactory. Doull and his collaborators,[8] Barenberg,[9] Mackay[10] and Colebrook,[11] in

2. Greider, C. E., and Downes, A. C.: Sunlight: Natural and Synthetic, Rep. Illum. Engin. Soc., Philadelphia, Sept. 24, 1929.

3. Sonne, C., and Rekling, E.: Treatment of Experimental Rat Rickets with Monochromatic Ultra-Violet Light, Strahlentherapie **25**:552, 1927.

4. Steenbock, H., and Black, A.: Induction of Growth-Promoting and Calcifying Properties in a Ration by Exposure to Ultra-Violet Light, J. Biol. Chem. **61**:405, 1924. Hess, A. F.: Experiments on the Action of Light in Relation to Rickets, Am. J. Dis. Child. **28**:517 (Oct.) 1924.

5. Hausser, K. W., and Vahle, W.: Strahlentherapie **13**:41, 1921.

6. Tisdall, F. F., and Brown, A.: Antirachitic Effect of Skyshine, Am. J. Dis. Child. **34**:737 (Nov.) 1927.

7. Maughan, G. H., and Smiley, D. F.: The Effect of General Irradiation with Ultra-Violet Light upon the Frequency of Colds, J. Prev. Med. **2**:69, 1928; Irradiation from a Quartz Mercury Vapor Lamp as a Factor in the Control of Common Colds, Am. J. Hyg. **9**:466, 1929.

8. Doull, J. A.; Hardy, Mary; Clark, J. H., and Herman, N. B.: The Effect of Irradiation with Ultra-Violet Light on the Frequency of Attacks of Upper Respiratory Disease (Common Colds), Am. J. Hyg. **13**:460, 1931.

9. Barenberg, L. H.; Friedman, I., and Green, D.: The Effect of Ultraviolet Irradiation on the Health of a Group of Infants, J. A. M. A. **87**:1114 (Oct 2) 1926. Barenberg, L. H., and Lewis, J. M.: The Effect of Carbon Arc Irradiation on the Health of a Group of Infants, ibid. **90**:504 (Feb. 18) 1928.

10. Mackay, H. M. M.: Artificial Light Therapy in Infancy, Arch. Dis. Childhood **2**:231, 1927.

11. Colebrook, Dora: Irradiation and Health: Ultra-Violet Irradiation of School Children; Irradiation of Varicose Ulcers, Medical Research Council, Special Report Series, no. 131, London, His Majesty's Stationery Office, 1929.

similar studies, came to the conclusion that irradiation did not lessen the number or severity of colds.

*Visible and Infra-Red Rays.*—Very little experimental work has been done to show what effect the portions of the spectrum other than the ultraviolet have on the growth and well-being of the animal organism. Sufficient has been done, however, to suggest that it is not correct to limit the therapeutic radiations to a narrow band between 290 and 302 mμ in the ultraviolet.

E. Luce Clausen [12] has recently shown that the exposure of rachitic rats to near infra-red radiation (from 720 to 1,120 mμ) for ten minutes daily causes considerable acceleration in growth, and Leonard Hill [13] was able to protect rabbits from lethal doses of staphylococcus by previous exposure to infra-red rays.

Sheard and Higgins [14] came to the conclusion that both visible and ultraviolet rays are essential for the normal growth and development of chicks. They claimed that infra-red radiation has no effect, but according to Clausen [12] they failed to exclude it from any of their filters, and consequently no conclusion as to its value is permissible from their data.

A number of reports indicate that there is an antagonistic action between the ultraviolet and the infra-red rays, or long visible rays. Hess,[15] working with rachitic rats, showed that an antagonism existed between the ultraviolet and the red end of the visible spectrum, but Steenbock and Black [16] could not confirm this. E. Luce Clausen [12] and also Bunker and Harris,[17] using the same technic, demonstrated an antagonistic action between the infra-red and the ultraviolet rays.

*Atmospheric Conditions Affecting Solar Radiation.*—Many factors influence the intensity of the solar radiation that reaches the earth.[18] Among the more important of these are the humidity of the atmosphere, the presence of clouds, the elevation of the sun, which varies with the

12. Clausen, E. M. Luce: The Effect of Infra-Red Rays on the Growth of Rachitic Rats, J. Nutrition **2**:125, 1929.

13. Hill, L., and Eidinow, A.: Protection Afforded by Short Infra-Red and Red Rays to Lethal Dose of Staphylococcus, Brit. M. J. **1**:388 (March 1) 1930.

14. Sheard, C., and Higgins, G. M.: Effect of Selective Solar Irradiation on the Growth and Development of Chicks, Am. J. Physiol. **85**:290, 1928.

15. Hess, A. F., and Weinstock, M.: A Study of Light Waves in Their Relation to Rickets, J. A. M. A. **80**:687 (March 10) 1923.

16. Steenbock, H., and Black, A.: Fat-Soluble Vitamins: Induction of Growth-Promoting and Calcifying Properties in Fats and Their Unsaponificable Constituents by Exposure to Light, J. Biol. Chem. **64**:263, 1925.

17. Bunker, J. W. M., and Harris, R. S.: Precise Evaluation of Light Therapy in Experimental Rickets, Am. J. Pub. Health **20**:1287, 1930.

18. Abbott, C. G.: The Sun, New York, D. Appleton and Company, 1911, p. 280.

season and the time of day, the altitude of the place and the amount of atmospheric pollution.

Kimball and Hand [19] have shown that in December and January there is over twice as much dust and smoke in the air of the city (Washington, D. C.) as there is in that of the suburbs. Shrader and his co-workers [20] found that the atmospheric pollution is one-sixth as great in the country as in the center of a city (Baltimore), and they conclude that there is a far greater amount (50 per cent more) of ultraviolet radiation in the country than in the city. They used photochemical methods. Tonney and his collaborators [21] reported similar results from observations made in Chicago.

It is probable that the intensities of the visible and infra-red rays are also influenced by the amount of atmospheric pollution. The experiments reported in this paper were carried out in the center of an industrial city, where the air contained considerable smoke and dust.

*The Therapeutic Value of Sunshine.*—The value of exposure to sunshine together with fresh air in the treatment of tuberculosis of the bones, joints and glands has been settled beyond dispute by Rollier [22] in Switzerland and Gauvain [23] in England.

There is, however, no uniformity of opinion as to which portions of the spectrum are essential in the treatment of tuberculosis. Jansen, Maar and Hasselbalck [24] and Phelps [25] are of the opinion that the long ultraviolet rays extending from 320 to 380 mμ exert the specific effect, and the last author is not convinced that radiation through window glass is ineffective.[26] Wright [27] suggested that with the aid of fluorescent substances, sunlight that has penetrated window glass might be converted into shorter wavelengths that would be of value in the healing of surgical tuberculosis. Finsen and Sonne [28] claimed that the visible rays are of special importance in the treatment of tuberculosis of the skin.

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19. Kimball and Hand: Monthly Weather Rev. **52**:133, 1924.

20. Shrader, J. H.; Coblentz, M. H., and Korff, F. A.: Effect of Atmospheric Pollution on the Incidence of Solar Ultra-Violet Light, Am. J. Pub. Health **19**: 717, 1929.

21. Tonney, F. O.; Hoeft, G. L., and Somers, P. P.: Loss of Actinic Intensity in Urban Sunshine Due to Air Pollution, J. Prev. Med. **4**:139, 1930.

22. Rollier, A.: Heliotherapy, New York, Oxford University Press, 1927.

23. Gauvain, H.: Sun Treatment in England, J. State Med. **38**:468, 1930; Clin. J. **59**:361, 1930.

24. Jansen, Maar and Hasselbalck, quoted by Reyn, A.: Light Treatment in Medicine, Radiology **4**:288, 1925.

25. Phelps, W. M.: Specificity of Light Action in Tuberculosis, J. Bone & Joint Surg. **12**:253, 1930.

26. Phelps, W. M.: Personal communication to the authors.

27. Wright, H. P.: Effect of Light in Treatment of Disease, M. Clin. North America **7**:1779, 1924.

28. Finsen, N. R., and Sonne, C., quoted by Reyn, A.: Light Treatment in Medicine, Radiology **4**:288, 1925.

Powers, Park, Shipley, McCollum and Simmonds [29] found that when rats on a diet deficient in vitamin A were exposed to sunlight xerophthalmia did not develop in them as soon or as severely as in controls that were either kept inside or exposed to a mercury vapor lamp, and they concluded that "Sunlight and out-of-door air with such factors as may be associated with them have wonderful health and life-giving properties, which enable the animal to adapt itself with a considerable degree of success to adverse environmental conditions."

In 1928, one of us (Dr. Robertson [30]) showed that the daily exposure of rats (on a rachitogenic diet) to direct sun's rays, in addition to the prevention of rickets, markedly increased their resistance to infection. It has been noted that exposure to cold air increases the tone and vigor of muscles and raises the rate of metabolism.[31] Gauvain,[23] Rollier,[22] Leonard Hill [32] and others gave considerable emphasis to the value of fresh air.

## EXPERIMENTS

Young albino rats were used as test animals in the following experiments. The breeding rats were kept on a normal diet that did not include any concentrated source of vitamin D, such as cod liver oil, and they were not exposed to any sunshine. At the beginning of each week litters that were from 25 to 27 days old were divided equally into five groups (of ten rats each), and three of these were placed on a modification of Steenbock's rachitogenic diet 2965,[16] which contained dried ordinary bread, 12.5 per cent; yellow corn, 59.5 per cent; wheat gluten, 17 per cent; wheat germ, 6 per cent; calcium carbonate, 3 per cent; sodium chloride, 1 per cent; machine-dried alfalfa, 1 per cent, and 2 cc. of strained tomato juice per rat every second day. The modification consisted in the substitution of bread for some of the corn and the addition of vitamins A, B, C and E in considerable quantities. The calcium-phosphorus ratio was 4:1. In twenty of the controls each week, 12.5 per cent of dried vitamin D bread [33] (which provided 3.5 Steenbock vitamin D units in 100 Gm. of the diet) replaced the ordinary bread, and of these, half were

29. Powers, G. F.; Park, E. A.; Shipley, P. G.; McCollum, E. V., and Simmonds, N.: Influence of Light and Darkness on the Development of Xerophthalmia in Rats, Proc. Soc. Exper. Biol. & Med. **20**:81, 1922.

30. Robertson, E. C.: A Study of the Effect of Various Agents, Chiefly Sunlight, upon the Susceptibility of Rachitic Rats to Infection, Am. J. Hyg. **9**:75, 1929.

31. Jakowenko, W. A.: Effect of Sun and Air Baths on the Respiratory Gaseous Exchange in Man, Am. J. Hyg. **10**:165, 1929; Ztschr. f. Hyg. **108**:259, 1928.

32. Hill, L.: Sunshine and Open Air, London, E. Arnold, 1924.

33. Tisdall, F. F.; Drake, T. G. H., and Brown, A.: The Incorporation of Vitamins in Bread, Canad. M. A. J. **24**:210, 1931.

kept inside and half put out under glass. By this method the viosterol was easily mixed evenly through the diet.

For the four weeks of sun-baths under glass, which were given on the roof of a five-story building, the rats were put out daily from 11 a. m. to 1 p. m., eastern standard time, except Sundays, in circular wire cages enclosed in square boxes made of common window glass. The boxes were open at two opposite sides, but as a similar empty glass box was fitted tightly on one open side and a wooden cover enclosing an electric fan on the other, very little, if any, unrefracted skyshine from near the horizon reached the rats (fig. 1). The sides of the boxes had to be removed in order to keep the rats sufficiently cool. If the weather was hot, the fan was turned on, and this sent a good current of air over the animals. The glass boxes and cages were covered with a large dark cloth while they were carried out and until they were placed in position. From February 17 to July 8 the rats under the

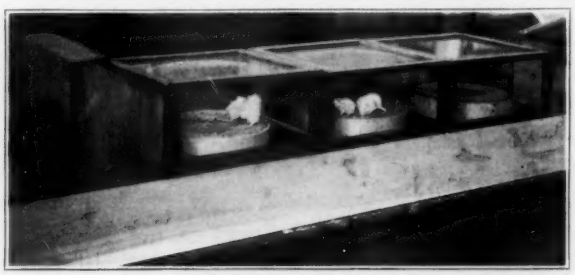

Fig. 1.—Apparatus for exposure of rats to fresh air and to sunshine through ordinary window glass.

glass boxes were put out in the direct sun (experiments 1 to 10 and 13 to 16). From the latter date until September 4, they were exposed to skyshine only; i. e., they were put out on the north side in the shade of a small building, because of the excessive heat of the direct sun. Tisdall and Brown [6] have shown that skyshine has over half the antirachitic effect of sunshine; this was later confirmed by Coblentz.[34] The rats in experiments 17, 18 and 22 received both sunshine and skyshine through glass. Those in experiments 19, 20 and 31 received only skyshine through glass. The rats were not put out on rainy days, and the total exposures to sunshine in the different experiments varied from twenty-five to thirty-six hours. Cotton sheets were hung in front of the cages in the animal room, so that no radiation through the windows could reach the rats.

34. Coblentz, W. W.: Transmissibility of Ultra-Violet Radiation, Nat. Tuberc. A. Tr. **24**:71, 1928.

The rats exposed to fresh air only were put out under wood instead of glass boxes, but all the other conditions were the same. Maximum and minimum thermometers were hung under one of the glass and one of the wooden cages, and readings were taken when the cages were taken in. In three of the preliminary experiments (which are not shown in table 1), in which the rats were put out on the roof in March and the first three weeks of April, the animals under the wooden boxes were subjected to temperatures varying from 40 to 50 F. on three days. They looked healthy and weighed as much as the others in the experiment, but none of them survived after they were given the infected broth, which indicates that this degree of cold markedly lowers the resistance of rats. In the subsequent experiments, on only six days

TABLE 1.—*Preliminary Experiments (Series 1) to Determine a Suitable Dose of "Rat Typhoid" Culture*

| Experiment | Bacterial Culture, Dose, Cc. | Modified Steenbock's Rachitogenic Diet | | | | | | | | | Modified Steenbock's Rachitogenic Diet with the Addition of Vitamin D | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Kept Inside | | | Exposed to Fresh Air Only | | | Sunshine Through Common Window Glass and Fresh Air | | | Kept Inside | | | Sunshine Through Common Window Glass and Fresh Air | | |
| | | Number of Rats | Number of Survivors | Percentage Survivors | Number of Rats | Number of Survivors | Percentage Survivors | Number of Rats | Number of Survivors | Percentage Survivors | Number of Rats | Number of Survivors | Percentage Survivors | Number of Rats | Number of Survivors | Percentage Survivors |
| 1–3 | 0.05 | 26 | 4 | 15.4 | .. | .. | .. | 25 | 10 | 40 | 26 | 11 | 42.3 | .. | .. | .. |
| 4–5 | 0.04 | 12 | 1 | 9.0 | 15 | 3 | 20 | 16 | 7 | 44 | 16 | 7 | 44.0 | 16 | 11 | 69 |
| 6–8 | 0.03 | 22 | 5 | 23.0 | 15 | 3 | 20 | 12 | 6 | 50 | 22 | 13 | 59.0 | 15 | 10 | 67 |
| 9–10 | 0.02 | 16 | 1 | 6.0 | 15 | 5 | 33 | 14 | 6 | 43 | 16 | 9 | 56.0 | 15 | 11 | 73 |

were the rats under the common window glass from 4 to 8 F. warmer than those under the wood, and probably, therefore, the temperature factor may be considered negligible. On omitting the three experiments in which the rats were too cold, the rats under the wooden boxes received the same amount of handling, exercise, fresh air and warmth as their litter mates under the glass boxes, and, therefore, the difference in survival rate between these two groups is due to the beneficial effect of the sun's radiation through glass.

The rats were weighed every week. In series 2 (table 2), at the end of the four weeks the rats on the rachitogenic diet exposed to the sun under window glass weighed on the average 71 Gm; those exposed to fresh air but no sun weighed 65 Gm. and those kept inside weighed 63 Gm. This difference in weight is unavoidable if divided litters are used, as in most cases all of the rats in the litter are of approximately the same weight when weaned. In half of the experiments in series 2, the rats kept inside varied within the same limits or

were heavier than those given irradiation under glass. Also, the weight of a rat is not necessarily an indication of its ability to survive the infection.

*Determination of the Degree of Rickets.*—After the four weeks were over, two representative rats were taken from each group, and the degree of rickets was estimated by the determination of the inorganic phosphorus in the whole blood [35] and the percentage of bone ash in the femora and tibiae [36] by Miss R. Herbert and Miss E. MacNamara. Roentgenograms were also taken of the bones of the legs (fig. 2). The

TABLE 2.—*The Effect of Sunshine Transmitted by Common Window Glass and of Fresh Air in Increasing the Resistance of Rats Fed a Rachitogenic Diet (with and without the Addition of Vitamin D) as Measured by the Percentage of Survivors*

| | | Modified Steenbock's Rachitogenic Diet | | | | | | | | | Modified Steenbock's Rachitogenic Diet with the Addition of Vitamin D | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Kept Inside | | | Exposed to Fresh Air Only | | | Sunshine Through Common Window Glass and Fresh Air | | | Kept Inside | | | Sunshine Through Common Window Glass and Fresh Air | | |
| Experiment | Bacterial Culture, Dose, Cc. | Number of Rats | Number of Survivors | Percentage Survivors | Number of Rats | Number of Survivors | Percentage Survivors | Number of Rats | Number of Survivors | Percentage Survivors | Number of Rats | Number of Survivors | Percentage Survivors | Number of Rats | Number of Survivors | Percentage Survivors |
| 13 | 0.01 | 8 | 2 | 25 | 8 | 4 | 50 | 8 | 3 | 38 | 7 | 4 | 57 | 8 | 5 | 63 |
| 14 | 0.01 | 7 | 1 | 14 | 8 | 4 | 50 | 6 | 3 | 50 | 8 | 6 | 75 | 8 | 6 | 75 |
| 15 | 0.01 | 9 | 3 | 33 | 6 | 2 | 33 | 7 | 4 | 57 | 8 | 4 | 50 | 8 | 6 | 75 |
| 16 | 0.01 | 6 | 2 | 33 | 7 | 3 | 43 | 6 | 3 | 50 | 6 | 3 | 50 | 3 | 3 | 100 |
| 17 | 0.01 | 5 | 2 | 40 | 8 | 3 | 37 | 7 | 4 | 57 | 6 | 3 | 50 | 7 | 6 | 86 |
| 18 | 0.01 | 6 | 2 | 33 | 6 | 4 | 66 | 8 | 6 | 75 | 7 | 5 | 72 | 8 | 8 | 100 |
| 19 | 0.01 | 7 | 3 | 43 | 8 | 3 | 37 | 8 | 5 | 63 | 6 | 4 | 66 | 7 | 5 | 72 |
| 20 | 0.01 | 8 | 3 | 37 | 6 | 3 | 50 | 8 | 5 | 63 | 8 | 5 | 63 | 8 | 6 | 75 |
| 21 | 0.01 | 8 | 3 | 37 | .. | .. | .. | 8 | 4 | 50 | 7 | 5 | 72 | 7 | 5 | 72 |
| 22 | 0.01 | 7 | 1 | 15 | 6 | 1 | 17 | 6 | 3 | 50 | 8 | 7 | 87 | 9 | 5 | 55 |
| Totals with standard deviation | | 71 | 22 | 32 ±10 | 63 | 27 | 43 ±14 | 72 | 40 | 57 ±10 | 71 | 46 | 61 ±10 | 73 | 55 | 75 ±15 |

values for the blood phosphorus of the rats on the rachitogenic diet are shown in table 3. There is little difference between the three groups. In the rats that received vitamin D in addition to the rachitogenic diet, the readings varied around 4 mg., whether the animals were kept inside or put out under glass. The percentage of ash in the bones of the rats on the rachitogenic diet is shown in table 4. The average of the figures in the first column (kept inside) and in the third column (exposed to sunshine under glass) are almost identical, which indicates that the severity of the rickets is not lessened by the sunshine through glass. The percentage of bone ash in both groups of rats that were

35. Tisdall, F. F.: J. Biol. Chem. **50**:329, 1922.

36. Bethke, R. M.; Steenbock, H., and Nelson, M. T.: J. Biol. Chem. **58**:71, 1923.

given vitamin D with their rachitic diet varied from 40 to 44. When the roentgenograms were examined, it was found that all of the rats on the rachitogenic diet, whether they were kept inside or exposed to fresh air or to sunshine under glass, showed rickets of the same severity ( fig. 2 *A* and *B*). There was no roentgen evidence of rickets in the rats that received the addition of vitamin D (fig. 2 *C*).

*Technic of Infection.*—At the end of the four weeks, the resistance of each rat to a culture of "rat typhoid" was tested in the following way: After a preliminary starvation period of eighteen hours, each rat was put in a small individual cage (fig. 3) and fed an accurately

Fig. 2.—*A*, roentgenogram of the leg of a rat kept inside. Note the marked rickets. *B*, roentgenogram of the leg of a rat fed a rachitogenic diet and exposed to fresh air and sunshine transmitted by common window glass. Note the marked rickets. *C*, roentgenogram of the leg of a rat kept inside and fed a rachitogenic diet with added vitamin D. There is no evidence of rickets.

measured amount of an eighteen hour broth culture of Salmonella muriotitis, on a cube of dried bread. Care was taken to see that all the bread was consumed, to make sure that the rat received the desired amount of culture. The organism is a strain of Salmonella enteritidis and was originally isolated from the infected middle ear of a white rat.[37] It is very pathogenic for young rats, as many of them succumb

37. McCordock, H. A.: A Bacillus of the Paratyphoid Group, Bull. Johns Hopkins Hosp. **37**:412, 1925.

in from seven to fourteen days with severe diarrhea, weakness, a bloody nasal discharge and terminal convulsions. Three fourths of the deaths in these experiments occurred within ten days after infection, and only 8 per cent of the deaths were after two weeks. The rats were not given any sunshine through glass or fresh air after infection.

Postmortem examinations were made on all the rats that died after the oral infection. The organs were examined, and cultures of

TABLE 3.—*Showing that the Inorganic Blood Phosphorus in the Rats Exposed to the Sunshine Transmitted by Common Window Glass Is Not Increased*

| | Modified Steenbock's Rachitogenic Diet | | |
|---|---|---|---|
| Experiment | Kept Inside | Exposed to Fresh Air Only | Sunshine Through Common Window Glass and Fresh Air |
| 13 | 1.1 | 1.2 | 2.0 |
| 14 | 2.0 | 2.3 | 1.8 |
| 15 | 2.2 | 2.5 | 2.1 |
| 16 | 1.6 | 3.3 | ... |
| 17 | 4.2 | 2.6 | 3.7 |
| 18 | 2.3 | 2.2 | 2.7 |
| 19 | 1.6 | 2.3 | 2.9 |
| 20 | 2.5 | 1.6 | 2.2 |
| 21 | 1.2 | ... | ... |
| 22 | 2.6 | 2.6 | 2.4 |

TABLE 4.—*Showing that the Percentage of Ash in the Bones of Rats Exposed to the Sunshine Transmitted by Common Window Glass Is Not Increased*

| | Modified Steenbock's Rachitogenic Diet | | |
|---|---|---|---|
| Experiment | Kept Inside | Exposed to Fresh Air Only | Sunshine Through Common Window Glass and Fresh Air |
| 13 | 25.3 | 20.3 | 31.3 |
| 14 | 29.2 | 34.1 | 30.7 |
| 15 | 32.8 | 32.5 | 34.6 |
| 16 | 27.0 | 24.1 | 35.0 |
| 17 | 33.7 | 37.1 | 25.6 |
| 18 | 31.9 | 34.6 | 30.9 |
| 19 | 26.5 | 28.1 | 29.8 |
| 20 | 38.0 | 33.7 | 37.1 |
| 21 | 30.0 | .... | 31.8 |
| 22 | 35.3 | 27.7 | 31.1 |
| Average | 31.0 | 30.0 | 30.8 |

the blood from the heart were plated on MacConkey's medium. In the majority of instances pure cultures of the typical clear colonies were obtained, indicating that the rat had muriotitis septicemia when it died. In a few cases the plates also showed colon bacilli. About one hundred and twenty of the recovered strains were tested by agglutination with S. muriotitis immune serum, and of these, all but three gave positive results in dilutions of 1:1,000 or over. The three negative cultures were not of S. muriotitis. In our previous experiments [38] about 1 per

38. Ross, J. R., and Robertson, E. C.: Increased Resistance of Rachitic Rats Exposed to Sunlight Through Vita Glass, Proc. Soc. Exper. Biol. & Med. **28**:443, 1931.

cent of several hundred cultures obtained in this way were not agglutinated by the immune serum; in other words, only about 1 per cent were not of S. muriotitis. The recovery, therefore, of pure cultures of clear colonies from MacConkey's medium can safely be considered to indicate that the rat died of a muriotitis infection. The occasional dead rats that did not yield S. muriotitis were considered as dying of nonspecific causes, and were omitted from the experiments.

All the rats were observed for four weeks after infection, when the experiments were terminated, and those that survived for this length of time are called survivors in the tables, and the degree of resistance in each experiment is estimated by the percentage of such survivors.

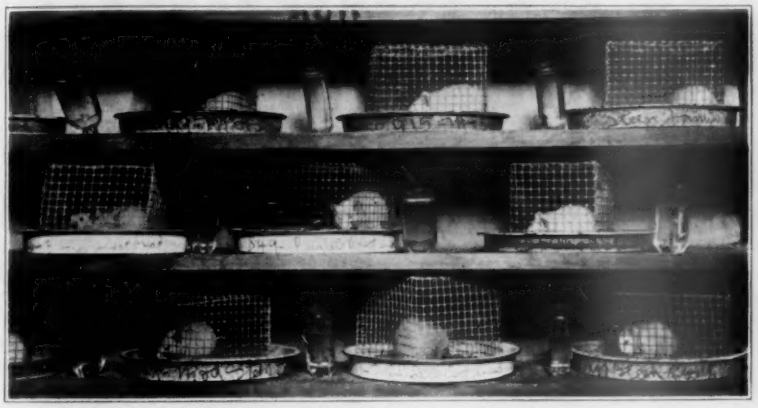

Fig. 3.—The individual cages used after infecting the rats.

## RESULTS

Several preliminary experiments were carried out with doses of the infected broth, varying from 0.05 to 0.02 cc. (given as 0.1 cc. of the proper dilution), with the results shown in table 1. In every experiment the rats that were given fresh air and sunshine through common window glass survived in greater numbers than the corresponding controls kept inside. Omitting the experiments in which the rats were too cold, it is seen that the rats exposed to fresh air survived better than those kept inside, except in one instance, but not as well as those exposed to fresh air and sunshine. This suggests that both the fresh air and the sunshine through glass increase the resistance.

It was decided to use 0.01 cc. as the standard dose, and table 2 gives the results in series 2. The results are consistent. With the rachitogenic diet the rats given sunshine filtered through glass always withstood the infection better than their litter mates kept inside. With the assistance of Dr. C. B. Weld, the results were statistically analyzed

according to the method described by Banister,[39] and the standard deviations [40] are given with the total percentages. Nearly twice as many of the rachitic rats exposed under common window glass (57 per cent) survived as of those kept inside (32 per cent), and statistically there is less than one chance in several hundred that these results are due to

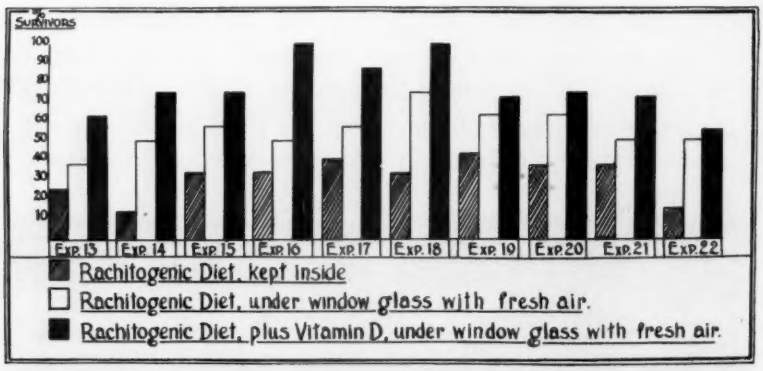


Fig. 4.—Percentage of survivors: (1) fed a rachitogenic diet and kept inside; (2) fed a rachitogenic diet and exposed to fresh air and to sunshine transmitted through ordinary window glass, and (3) fed a rachitogenic diet with added vitamin D and exposed to fresh air and sunshine transmitted through ordinary window glass.

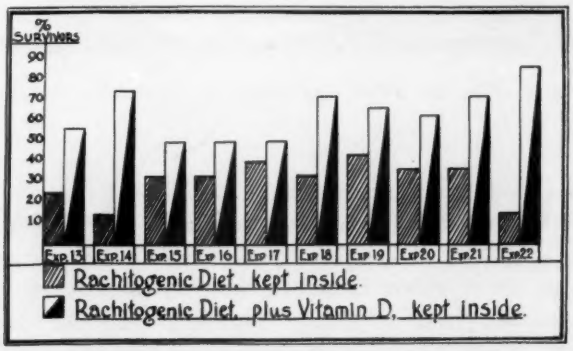


Fig. 5.—Percentage of survivors: (1) fed a rachitogenic diet and kept inside; (2) fed a rachitogenic diet, plus vitamin D and kept inside.

coincidence. These results are shown graphically in figure 4. The rats exposed to fresh air showed more variation, but the average (43 per cent) is about midway between the average of the group given sunshine

39. Banister, H.: Elementary Applications of Statistical Method, London, Blackie, 1929, pp. 19 and 29.

40. The probable error is about two thirds of the standard deviation.

through glass and that of the group kept inside. When vitamin D was added to the rachitogenic diet, the beneficial effect of exposure to fresh air and sunshine through window glass was still evident, as 61 per cent of those kept inside survived as compared with 75 per cent of those exposed under glass.

Also, the addition of vitamin D increases the ability of the rats to withstand this infection (fig. 5). Of the rats that were kept inside, 32 per cent of those on the rachitogenic diet lived, as compared with 61 per cent of those that were given vitamin D in addition. There is less

TABLE 5.—*Effect of Fresh Air and Sunshine Through Common Window Glass (Read Down)*

| | Percentage Survivors | |
|---|---|---|
| | Rachitogenic Diet | Rachitogenic Diet with Addition of Vitamin D |
| Kept inside | 32 | 61 |
| Exposed to fresh air and sunshine through common window glass | 57 | 75 |

TABLE 6.—*Effect of the Addition of Vitamin D (Read Down)*

| | Percentage Survivors | |
|---|---|---|
| | Kept Inside | Exposed to Fresh Air and Sunshine Through Common Window Glass |
| Rachitogenic diet | 32 | 57 |
| Rachitogenic diet with addition of vitamin D | 61 | 75 |

TABLE 7.—*Percentage of Transmissions of Various Lines in the Ultraviolet*

| Sample | Thickness, Mm. | 302 Microns | 313 Microns | 334 Microns | 365 Microns |
|---|---|---|---|---|---|
| No. 1 | 2.30 | 0.0 | 2.0 | 44.5 | 86.0 |
| No. 2 | 2.13 | 0.0 | 2.5 | 47.0 | 86.5 |
| American window glass | 2.26 | 0.0 | 6.0 | 57.0 | 87.0 |

than one chance in several hundred that these results are due to coincidence. This confirms our previous work.[41] Of the rats that were put out in the sun under glass, 57 per cent of those on the rachitogenic lived as compared with 75 per cent of those that were given vitamin D in addition (fig. 4). There is less than one chance in a hundred that these results are statistically insignificant.

The results are consistent throughout, as the beneficial effect of exposure to fresh air and sunshine through window glass is evident whether vitamin D is absent or present in the diet (table 5), and the beneficial effect of vitamin D is evident whether the rats are kept

41. Robertson, E. C., and Ross, J. R.: Increased Resistance of Rachitic Rats Fed Irradiated Food, Proc. Soc. Exper. Biol. & Med. **27**:999, 1930.

inside or exposed outside to sunshine through common window glass (table 6). By the beneficial effect is meant the increased ability of the animals to withstand the infection.

### TRANSPARENCY OF THE GLASS FOR ULTRAVIOLET AND INFRA-RED RAYS

The percentage transmissions in the ultraviolet of two samples of the glass used in these experiments (samples 1 and 2, table 7) and an average sample of American window glass were determined by Dr. W. W. Coblentz of the Bureau of Standards, Washington D. C. The measurements were made with a thermopile and galvanometer, and the source of light was a mercury vapor lamp. The percentage transmissions (table 7) of all three samples are practically the same. The window glass commonly used in Canada is manufactured in Belgium

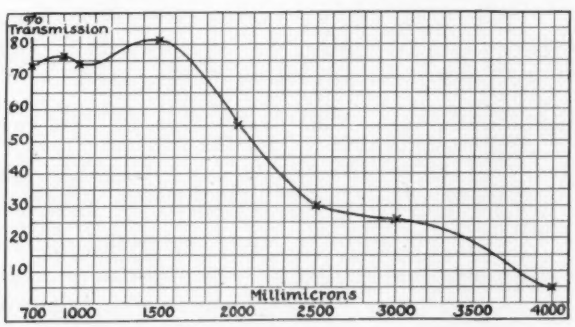


Fig. 6.—The percentage of infra-red rays that are transmitted by the window glass that was used in the experiments.

or Czecho-Slovakia, and the pieces we used were imported from the former country.

The energy curve for the transmission of the infra-red rays through the window glass (as determined by the thermopile and galvanometer method) is shown in figure 6. These determinations were made by Mr. H. J. C. Ireton and Miss E. J. Allin of the department of physics, University of Toronto. The maximum transmission is at 1,500 mμ, and from this point it gradually decreases, until at 4,000 mμ it is 5 per cent.

### COMMENT

Dust or dirt on the surface of glass greatly reduces its power to transmit solar rays. For example, Coblentz [42] showed that a piece of

42. Coblentz, W. W., and Stair, R.: Data on Ultra-Violet Solar Radiation and the Solarization of Window Materials, Bureau of Standards, J. Research **3**:653, 1929.

window glass when clean transmitted from two to two and a half times as much short ultraviolet (302 line) as the same piece after it had been left outdoors for three months. Even a small amount of dust will decrease the transmission by 10 per cent. The glass boxes in our experiments were cleaned about once a week, and would, therefore, be comparable to household windows.

Common window glass is opaque to the very short ultraviolet and to the long infra-red beyond 4,000 mμ, but it transmits the rest of the solar spectrum, that is, the long ultraviolet (above 313 mμ), the visible and the shorter infra-red. We are unable to state whether all of these rays or only one particular region is responsible for the increased resistance of the animals.

## CONCLUSIONS

1. The addition of vitamin D to a rachitogenic diet (that already contains considerable quantities of the other vitamins) markedly raises the resistance of rats to infection.

2. Exposure to sunshine transmitted by common window glass and to fresh air, for a comparatively short period daily, markedly raises the resistance of rats to an oral enteritidis infection, whether they are fed a rachitogenic diet or a rachitogenic diet plus vitamin D.

3. When the rachitogenic diet is used, the increased resistance is not due to any improvement in the rickets, as the sunshine that passes through the common window glass has no antirachitic effect.

4. Exposure to fresh air alone has about half the beneficial effect of the combination of fresh air and sunshine through glass, as measured by the ability of the rat to withstand infection.

5. The vital radiations from the sun should not be limited to the narrow band in the short ultraviolet region, which is antirachitic. The foregoing results show definitely that rays longer than those that are necessary to prevent or cure rickets have a marked effect on the animal organism, as evidenced by a decided increase in resistance to infection.

# EFFECTS OF COD LIVER OIL—SKIMMED MILK FEEDING ON BONES OF INFANTS

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Various observers have reported that the osseous manifestations of rickets are about as frequent in children who have received cod liver oil treatment as in those who are untreated. Eliot[1] in a series of 103 infants found that of those receiving cod liver oil in doses of 3.6 ounces (102 Gm.) per month for twelve months (averaging 1 teaspoonful per day), 37 per cent showed complete control of rickets and 62 per cent showed partial control, whereas of those without cod liver oil at 13 months, 21 per cent had indifferent control, and 74.5 per cent partial control and 7 per cent showed complete control. She said:

> That rickets is intimately associated with growth is well known and that it should appear at the time when most active growth is taking place, namely, the first four months of life, is not extraordinary. The rate of growth of the infant influences the early development of the disease. Large, rapidly growing breast-fed infants and very fat infants show definite evidence of rickets.

Wilson,[2] in a study of infants aged from 1 to 3 months, born in the spring, receiving doses of from ½ to 1½ teaspoonfuls of a biologically tested cod liver oil daily, reported the development of clinical rickets in 91 per cent of the subjects. A more intensive study of 47 infants, aged from 2 weeks, born in the winter of 1925, receiving daily doses of 1, 2 and 3 teaspoonfuls of biologically tested cod liver oil showed the development of clinical rickets in 68 per cent of the cases as compared with 76 per cent of the control series of 30 cases. Dr. Wilson concluded that the nature of the relation of cod liver oil therapy to the development of rickets as observed in these studies would seem to be one of control rather than of prevention.

Mitchell and Nelson,[3] in a study of 150 infants from 3 to 12 months of age, showed that in 77 per cent receiving no cod liver oil rickets developed, and that 69 per cent of those receiving less than 1 teaspoonful and 79 per cent of those receiving more than 1 teaspoonful had rickets. They stated:

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From the University Hospital.

1. Eliot, M. M.: Control of Rickets, J. A. M. A. **85**:656 (Aug. 29) 1925.
2. Wilson, May G.: The Prevention of Rickets, Am. J. Dis. Child. **31**:603 (May) 1926.
3. Mitchell, Edward Clay, and Nelson, M. V.: Growth of Bone and Development of Rickets, J. A. M. A. **95**:1896 (Dec. 20) 1930.

Much has been said of the rickets produced by rapid growth, but should it be necessary to stunt infants in order to prevent the development of rickets? Should not the infant be allowed to gain as he will, provided his food intake is properly balanced? It may be that one teaspoonful of cod liver oil is an adequate amount for a rapidly growing infant, but we believe one should consider not only whether or not the infants grow too rapidly or receive too little cod liver oil, but also whether these minor bone changes in the early months of life are rachitic in nature.

To determine whether the various reports showing the presence of rachitic conditions after giving cod liver oil to infants were due to insufficient dosage of cod liver oil, I placed a group of infants on a diet in which the whole fat intake was standardized cod liver oil. This was done by skimming the cream from the milk and adding 3 per cent of cod liver oil. Cereal, water and cane sugar were added to make a formula, according to the approximate method of Budin, which allows from 1½ to 2 fluid ounces (45 to 60 cc.) of whole boiled milk plus 1/10 ounce (3 Gm.) of sugar to a pound (453.6 Gm.) of body weight until that weight is 20 pounds (9,071.8 Gm.). Vegetables, orange juice and cereal were fed as is usual in infant feeding. I have shown in a previous paper that this diet is well taken, promotes rapid growth and produces a placid, nonnervous infant that resists infections well. The amount of cod liver oil taken daily varied with the weight of the child, being always 3 per cent of the milk. Therefore, when the child weighed 10 pounds (4,535.9 Gm.) and was taking 1 pint (473 cc.) of milk, the daily amount of cod liver oil was 4 teaspoonfuls, and at 21 pounds (9,525.6 Gm.), when he was taking 1 quart of milk, he received 8 teaspoonfuls, or 1 ounce (28.34 Gm.), of cod liver oil daily. These doses are much larger than those usually recommended.

This report deals with the clinical and roentgenographic findings after several months of this type of feeding. The infants were white and were reared in private homes of the better kind. No ultraviolet radiation or viosterol was used.

## REPORT OF CASES

CASE 1.—E. H., born Nov. 17, 1928, with a birth weight of 7 pounds and 8 ounces (3,401.9 Gm.), had no breast milk from birth. At the age of 3 weeks, weighing 7 pounds and 9 ounces (3,430.3 Gm.), he seemed a normal infant. The diet was continued throughout the first year. Gain in weight was rapid, at 10 months the weight being the average for a 1 year old child. At 1 year he weighed 22 pounds and 9 ounces (10,234.17 Gm.), was 1 inch (2.5 cm.) over the average height (30 inches [76.2 cm.]). He walked at 10 months. At 1 year, the anterior fontanel was 1 inch (2.5 cm.) in diameter (normal), and he had nine teeth. Rachitic signs were moderate but distinct. There were enlargement of the frontal and costal bosses, enlarged epiphyses, moderate Harrison's groove and mild bilateral genu varus. As early as 3 months it was noted that the costal and frontal bosses were enlarged. During the year he had four infections of the upper respira-

tory tract, of which three were afebrile, and in one there was a temperature of 102 F. for one evening. His color, activity and disposition were good. He slept much and quietly and was never constipated.

The roentgenogram taken at the age of 1 year showed good ossification, the radial and ulnar epiphyses being broadened and flared. The roentgenologist made a diagnosis of healed rickets. Six months later, with the child on the same diet, the roentgenograms showed no genu varus. The bones of the legs showed good ossification with "mushroom" ends, usually diagnosed as healed rickets.

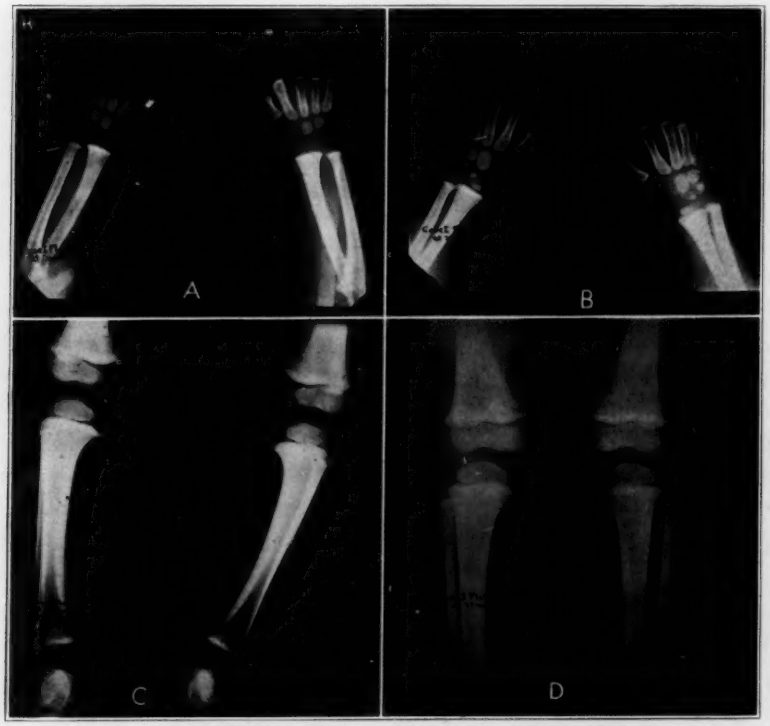


Fig. 1.—Roentgenograms in case 1: *A*, at 1 year; heavily calcified shafts with the periphery accentuated; lipping and spreading of carpal diaphyses of radius and ulna. *B*, at 27 months; calcification marked; ends of diaphyses spread and lipped. *C*, at 18 months; lipping and mushrooming of femurs and tibial diaphyseal ends; right genu varus. *D*, at 27 months; spreading of diaphyseal ends with lipping; genu varus not present.

Case 2.—Y. R., born June 27, 1929, weighing 8 pounds (3,628.7 Gm.), was breast fed for six weeks and then bottle fed. At 3 months he weighed 11 pounds and 6½ ounces (5,173.8 Gm., a normal gain). He was placed on the diet. At 13 months he weighed 28 pounds (12,700.6 Gm.), 6½ pounds (2,954.3 Gm.) above the average. He had seven teeth; the anterior fontanel measured 1 inch (2.5 cm.). There were visibly enlarged costal and frontal bosses, a moderate Harrison's

groove and genu varus. He walked at 16 months. He had two afebrile infections of the upper respiratory tract. At no time did he display any nervous signs; he was never fretful, and slept much and quietly.

Roentgenograms taken at 1 year showed good calcification with enlarged flaring epiphyses diagnosed as healed rickets. No genu varus was evident in the roentgenograms.

CASE 3.—E. W., born Aug. 28, 1928, weighing 7 pounds and 10 ounces (3,458.6 Gm.), was bottle fed from birth. At 3 months he weighed 12 pounds and 10

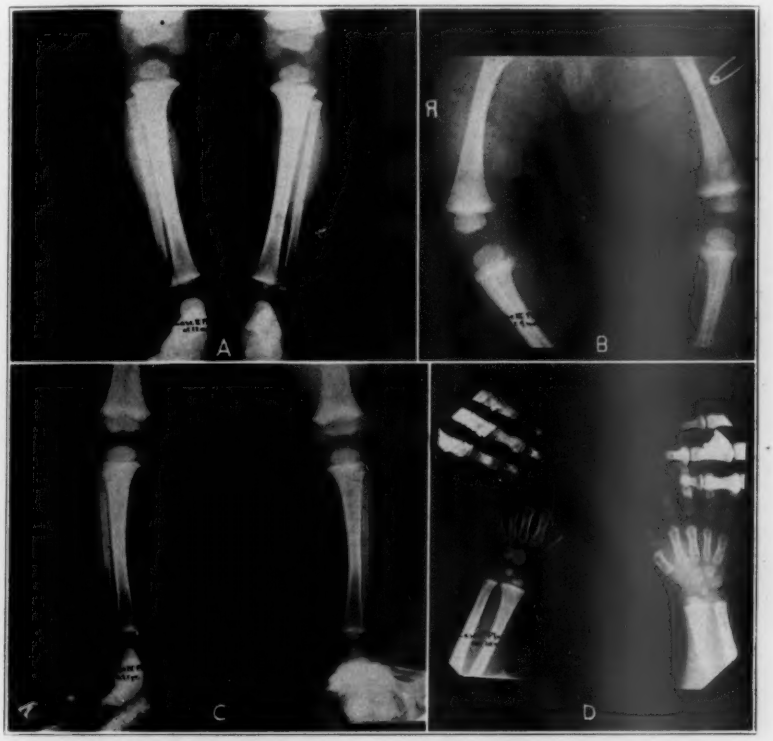


Fig. 2.—*A,* roentgenogram in case 2, at 13 months. Diaphyseal ends show spreading and lipping; genu varus not present. *B,* in case 3, at 9 months. Genu varus; anterior bowing of right femur; mushrooming and lippings. *C,* in case 4, at 1 year. Lower diaphyseal ends of fibula and tibia not lipped nor spread. *D,* in case 5, at 21 months. Doubtful lipping and spreading.

ounces (5,726.6 Gm.), an excess gain since birth of 20 ounces (567 Gm.). At that time, he was taking 30 fluid ounces of whole milk with 6 teaspoonfuls of dextromaltose and ½ teaspoonful of cod liver oil daily. He had a discharging otitis media of one day's duration. Enlarged epiphyses and frontal and costal bones showed beginning rickets. The diet was started at once, and he gained 5 pounds (2,267.9 Gm.) in eleven weeks, an average of over 7 ounces (198 Gm.) a week. He weighed 21 pounds (9,525.4 Gm.) at 8 months. At 1 year he had seven teeth, weighed 26 pounds (11,793.4 Gm.), was 30½ inches (77.5 cm.) tall and stood

alone, and the anterior fontanel was closed. He showed enlarged costal and frontal bosses with enlarged epiphyses, moderate Harrison's groove, genu varus and anterior bowing of the femurs. He had had three infections of the upper respiratory tract, one with peritonsillar abscess and one with a second discharging otitis media. He was placid in disposition, slept well when not ill and needed extract of malt constantly in his diet to prevent constipation.

The roentgenograms at 9 months showed "mushrooming" of the ends of the femurs and the upper and lower ends of the tibiae and fibulae, with some anterior bowing of both the right and the left femur shafts and genu varus.

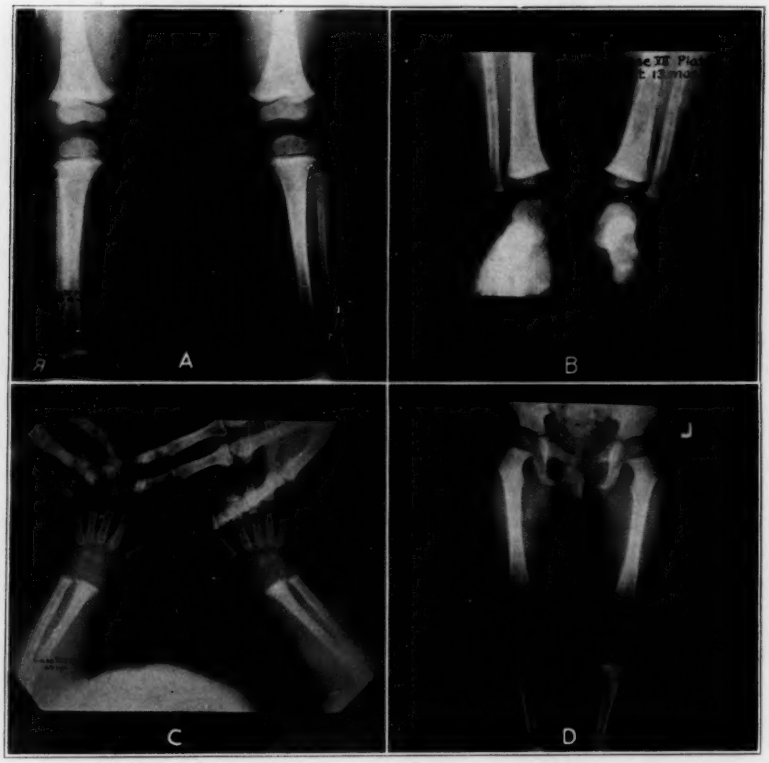


Fig. 3.—*A,* roentgenogram in case 6, at 18 months. No genu varus; mushrooming of diaphyseal ends of femurs and upper ends of tibias; lipping and cupping of lower ends of tibias and fibulas interpreted as active rickets. *B,* in case 7, at 13 months. Lipping and spreading of diaphyseal ends of fibulas and tibias. *C,* in case 7, at 1 year. Lipping and spreading of diaphyseal ends of ulna and radius. *D,* in case 7 at 1 year. No genu varus; moderate spreading and lipping of diaphyseal ends.

The diet was continued, and the bowing of the knees had entirely disappeared at 18 months. The bosses appeared less prominent.

Case 4.—P. B., born March 18, 1929, weighing 6 pounds and 4 ounces (2,840.95 Gm.), at 7 weeks weighed 9 pounds and 1 ounce (4,110.6 Gm.), 15 ounces

(4.25 Gm.) over the average gain. She was normal, except for a hernia of the navel. She was receiving 1 fluid ounce of milk at a nursing from the breast; the breast milk failed entirely at 3 months. She was placed on the diet as a supplementary feeding at first, and then entirely after the breast milk failed. Her gain in weight was not excessive, about 5 ounces (141 Gm.) a week, and at 1 year she weighed 21 pounds and 13 ounces (9,440.38 Gm.), her height was 29 inches (73.66 cm.), the anterior fontanel was ½ inch (1.27 cm.) wide, and she had five teeth. The costal bosses were hard and small; there were some flaring of the costal arch and a moderate Harrison's groove. She stood alone and walked at 14 months. A marked tendency to constipation was relieved by substitution of extract of malt for part of the cane sugar. There were two mild infections of the upper respiratory tract. Her sleep was unbroken; she ate willingly, and was a quiet, happy child. The roentgenograms at 1 year showed "normal" epiphyses.

Fig. 4.—Hypercalcification after administration of large doses of viosterol to a normal infant (after Alfred Hess).

Case 5.—J. F., born Sept. 16, 1929, weighing 6 pounds and 10 ounces (3,011 Gm.), was breast fed, with complementary feeding from birth; no vitamin D therapy was given until the end of the third week, when the diet was started. At 1 year he weighed 21 pounds and 6 ounces (9,695.5 Gm.) and had six teeth; the anterior fontanel was open 1 inch; there were visible bosses, mild genu varus and mild Harrison's groove. At 19 months the bones were nearly normal clinically and roentgenographically. The child weighed 27 pounds (12,246.9), was 33 inches (83.82 cm.) tall, had sixteen teeth and was a robust, ruddy boy.

Case 6.—R. N., born prematurely on Jan. 17, 1928, at the eighth month, weighing 5 pounds (2,267.9 Gm.), was presented at 6 weeks. He was placed on the skimmed milk-cod liver oil diet. At 18 months he weighed 25 pounds and 8 ounces

(11,566.6 Gm.), and showed hard, discrete frontal and costal bosses, and a mild Harrison's groove. There was no bowing of the legs. He had ten teeth, but the canines were delayed.

Roentgenograms showed enlarged epiphyses. The lower ends of the tibiae were lipped and cupped with heavily calcified diaphyses, indicative of healing rickets.

CASE 7.—C. L., born May 21, 1929, at the seventh month of pregnancy, weighing 3 pounds (1,814.3 Gm.), was breast fed. She was first seen on July 18, 1929, weighing 4 pounds and 1 ounce (1,842.72 Gm.), a gain of 17 ounces (481.5 Gm.) in nine weeks. Condensed milk was added as a supplementary feeding. On Oct. 10, 1929, at the age of 5 months, the child weighed 8 pounds and 4 ounces (3,742.1 Gm.), and was placed on a skimmed milk-cod liver oil diet. She gained 22 ounces (623.7 Gm.) the first month, 20 ounces (567 Gm.) the second month, and 28 ounces (793.8 Gm.) in the next six weeks, and at 13 months her weight was 17 pounds and 15 ounces (8,136.31 Gm.). She had two teeth, and the anterior fontanel was closed. She could creep and speak a few words. There was a mild Harrison's groove, but no symptoms of disturbance of the nervous system.

*Summary of Clinical Findings*

| Case | 1 | 2 | 3 | 4 | 5 | 6 | 7* |
|---|---|---|---|---|---|---|---|
| Sex | M | M | M | F | M | M | F |
| Birth Weight (pounds) | 7.8 | 8 | 7.10 | 6.4 | 6.10 | 5 | 3 |
| Time on Diet (months) | 12 | 9 | 9 | 9 | 12 | 16 | 8 |
| At 1 Year Weight (pounds) | 22 | 28 | 26 | 21 | 21 | 22 | 17 |
| Height (inches) | 30 | 32 | 30½ | 29 | 29 | 30 | 25 |
| Anterior Fontanel (inches) | 1 | 1 | 0 | 1½ | 1 | ½ | 0 |
| Teeth | 9 | 7 | 7 | 5 | 6 | 6 | 2 |
| Bosses Frontal Costal | + | + | + | + | ± | ± | + |
| Enlarged Epiphyses | + | + | + | + | ± | ± | + |
| Harrison's Groove | + | + | + | + | + | + | + |
| Genu Varus | + | + | + | 0 | + | 0 | 0 |
| Anterior Bowing of Femur | 0 | + | + | 0 | 0 | 0 | 0 |

* Premature.

The roentgenograms taken at 13 months showed mushrooming and flaring of the femurs and ends of the tibiae and fibulae.

## COMMENT

It will be noted in these cases that, from the clinical point of view, the osseous findings ordinarily called rachitic were present in greater number and degree than usual in children who have received smaller doses of cod liver oil, and that these findings were most exaggerated in children who were most over the average weight at 1 year. These results inspire the question as to whether such findings are partially or wholly a normal variant, in larger children, of the bulbous enlargements of the growth centers in flat bones and the ends of the long bones. Are the more rapidly growing, larger children normally possessed of such larger bone tuberosities?

The roentgen findings here diagnosed as healed rickets, in accordance with the text and plates of Koehler, are apparently indistinguishable

from those shown by Alfred Hess as an example of hypercalcification due to large doses of irradiated cholesterol.

Despite the presence of enlarged bosses and flexures, such as moderate bowing at the knee joint, moderate anterior bowing of the femurs and Harrison's groove, there is something that does not seem rachitic in these cases. A diagnosis of rickets, like most medical judgments, is based on the history and the clinical and laboratory findings. There is nothing deprivative in the calcium, phosphorus or vitamin intake. The essential nature of rickets "must be regarded not as a result of a failure of calcification but as a disorder characterized by specific changes in the preparatory cartilage and in the growing tissue" (Alfred Hess). "A marked increase in calcification of the long bones (subepiphyseal band) took place (after phosphorus) concurrently with the development of typical rachitic lesions" (Hess [4]). Therefore, the process in the diaphyseal ends, as shown in roentgenograms, indicates in active rickets the delay in ossification of the center of the diaphyseal end as a cupping as compared to the undelayed growth and calcification in the periphery, where unrestricted periosteal bone growth evinces itself by "lipping."

In healing rickets, the delayed process calcifies rapidly and "growth attains not only the normal rate but becomes excessive." Apparently both the central and the peripheral growth are such that the predominance of peripheral growth persists, shown in roentgenograms as spreading, mushrooming, broadening or flaring, as the process is variously termed.

With hypertrophy and hypercalcification, there is again disparity of growth between the center and the periphery, possible because of the time element necessary to complete the complicated process of conversion of cartilage into bone as compared with the relatively simple process of direct periosteal ossification.

In rickets, the disparity is due to the delay produced by vitamin D deprivation, causing failure of calcification, and in hypertrophy with hypercalcification the disparity is due to great and unequal stimulation in which one process is unable to keep pace with the other. The result again is great prominence of the peripheral growth, seen in roentgenograms as flaring, spreading, broadening and mushrooming.

The many concomitant and associated factors of rickets are entirely lacking in these cases, as will be noted by the absence of symptoms of disturbance of the nervous system, the somewhat early appearance of teeth and the smaller than normal size of the fontanels.

Summarizing these cases, the outstanding features are the absence of symptoms of the nervous system, the ruddy robust appearance and

4. Hess, A. F., and Weinstock, M.: The Value of Elementary Phosphorus in Rickets, Am. J. Dis. Child. **32**:483 (Oct.) 1926. Hess, A. F.: Rickets, Osteomalacia, and Tetany, Philadelphia, Lea & Febiger, 1929.

the large gains in weight. All the patients showed enlarged frontal and costal bosses and some flaring, broadening or spreading of the diaphyseal ends; four of them showed transitory bowing of the legs.

The roentgenograms of infants who were overweight showed relative enlargement of the diaphyses, interpreted as healed rickets. One film (case 5) may be read as still showing some of the "fraying" of active rickets.

It will be noted that the degree of rachitic findings in the bones was greatest in those children who were most overweight at 1 year.

My clinical impression was that the degree and frequency of these so-called rachitic findings were much greater in this series than is usually seen in infants given smaller doses of cod liver oil. This accords with the previous findings of Eliot,[1] Wilson [2] and Mitchell and Nelson [3] that hypertrophic (rachitic) osseous findings are greater in children to whom cod liver oil has been given. These findings suggest the probability of the truth of the conclusion that, so far as cod liver oil contributes to the overgrowth of the infant, it is an etiologic factor in the causation of certain hypertrophic manifestations undifferentiable from those of healed rickets. The conditions shown in the roentgenograms in these cases are more correctly interpreted as hypertrophy with hypercalcification than as healed rickets. These results demonstrate the futility of endeavoring to prevent these findings by massive doses of cod liver oil, and prompt the suggestion that the avoidance of overgrowth will prove more efficacious in preventing these findings, if this prevention is clinically desirable.

# Case Reports

## EXTENSIVE DECALCIFICATION OF THE BONES IN AN EIGHT YEAR OLD BOY

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The following case, which has been observed for four years, is one of an unusual type of decalcification of the bones in an 8 year old boy. A decreased calcium content of bone brings to mind the following conditions in which it tends to occur: osteitis fibrosa cystica, rickets, renal rickets, osteomalacia, hyperthyroidism, ammonium chloride and acid poisoning, atrophy of disuse and osteoporosis due to a low calcium and phosphorus intake. The case to be described does not readily fall into any of these categories.

### REPORT OF A CASE

W. R., aged 4 years, was first admitted to the Lenox Hill Hospital on Dec. 22, 1927, because of a reducible right inguinal hernia which had been growing larger since birth. He had lived in New York all his life. Both parents, Porto Rican by birth, were well. The mother had never had a miscarriage. The patient had four brothers and sisters, the eldest of whom, a girl of 6, had tuberculous glands. He was normally delivered at term, and was breast fed for two months. Orange juice was administered at the age of 8 months, and cod liver oil was given sporadically after the first year. He walked at the age of 19 months. The first tooth appeared at 9 months, and there were four teeth at the end of that year. Measles and chickenpox were the only two illnesses experienced up to the time of admission.

The patient was pale and undernourished, weighing 26¾ pounds (12.1 Kg.). He was a mouth breather and had marked hypertrophy of the tonsils. There were very definite stigmas of rickets: a marked rachitic rosary, Harrison's groove, slight prominence of the frontal bones, extreme enlargement of the epiphyses of the wrists, some enlargement of the ankles and bowing of the lower extremities. A right reducible inguinal hernia was present. The remainder of the physical examination gave essentially negative results. The urine was normal. On Dec. 28, 1927, the tonsils and adenoids were removed. A right indirect inguinal hernia was repaired on Jan. 12, 1928. The patient's stay in the hospital was uneventful, and he was discharged on Feb. 11, 1928.

Because of the deformity of the lower extremities, the patient was readmitted on Nov. 20, 1928. He had had pertussis eight months before. The deformities of the lower extremities were striking. There was marked bowing of both femora, the curvature being not only outward but anterior. Equally impressive were the forward bowing of both tibiae and the bilateral genu valgum. These

From the A. Jacobi Division for Children of the Lenox Hill Hospital.

deformities were confirmed by roentgen examination, and in addition lateral bowing of both radii was observed. Further, roentgen examination revealed marked rarefaction of the lower thirds of the femora and the distal epiphyses. There were pronounced thinning of the cortex, coarsening of the trabeculae and very suggestive cysts in the medulla. The central thirds of the bones, in the region of the greatest bowing, showed thickening of the cortex. The tibiae showed similar changes in the proximal and distal thirds—rarefaction, thinning of the cortex and vacuolization of the medulla, with thickening of the cortex in the severely bowed middle third. There was disorganization of the architecture of the distal metaphyses of the ulnae. The roentgenographic findings were highly suggestive

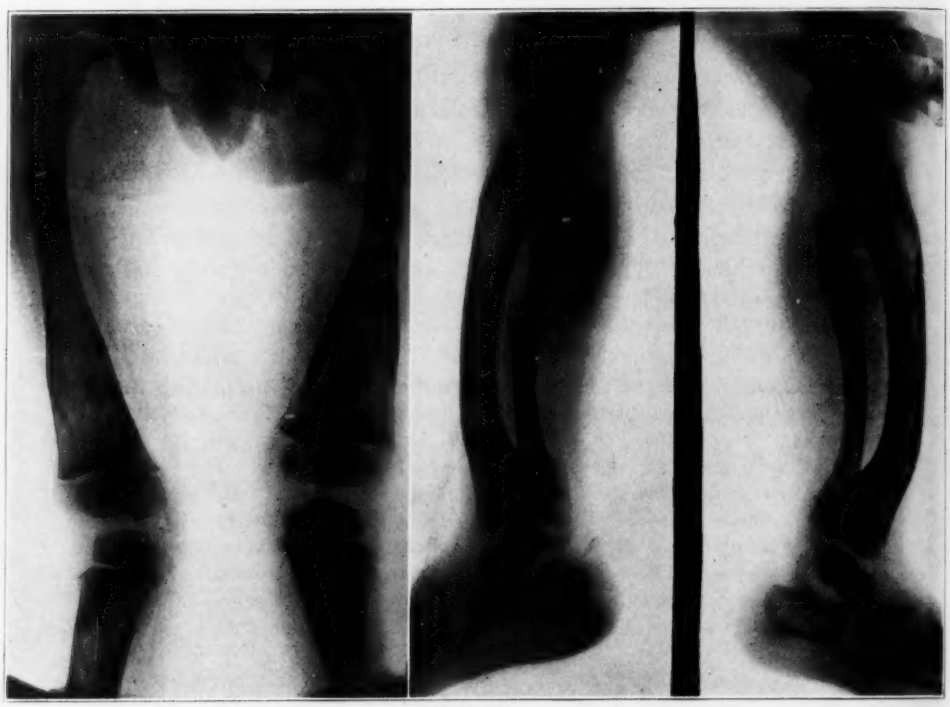

Fig. 1.—Roentgenograms of the lower extremities, taken in 1928. Note the bowing of the bones. The thinning of the cortex, the areas of rarefaction and the suggestive cystic changes in the lower third of the femora and the upper and lower thirds of the tibiae are clearly shown.

of osteitis fibrosa cystica (fig. 1). The Wassermann tests of the blood of the patient and mother were negative. The boy's serum calcium was 10.8 mg. per hundred cubic centimeters. The routine tests of the urine repeatedly gave negative results. The weight varied between 31 and 34 pounds (14 and 14.5 Kg.). The patient was discharged on Jan. 17, 1929.

On May 9, 1929, the patient was admitted for surgical correction of the genu valgum. Although the generalized nature of the condition was well realized, the deformity was so marked that a bilateral supracondylar osteotomy was deemed necessary. The operation was performed on May 14, and one month later, when

the plaster casts were finally removed, firm union had taken place and the deformity was corrected. This was confirmed by roentgen examination. Dr. Frederick Bullock made the following report on the microscopic examination of two specimens of bone removed from the distal metaphyses of the femora at the time of operation: "Sections of the decalcified bone show widening of the marrow spaces with rarefaction of the trabeculae. The marrow is for the most part of

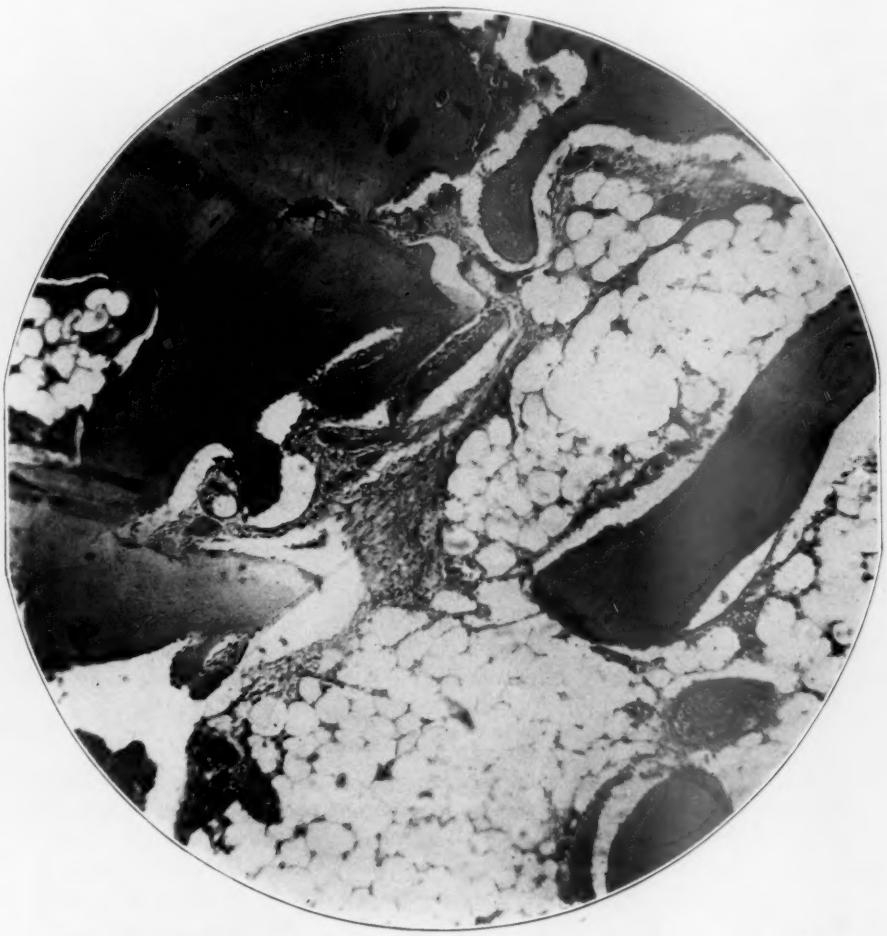

Fig. 2.—Photomicrograph of a section of bone removed from the distal metaphysis of the femur (low power magnification). Note the rarefaction of the trabeculae, the widening of the fatty marrow spaces and the small area of loose vascular granulation tissue in the center of the photograph.

the ordinary fatty type, though in localized areas it is fairly rich in cells. Osteoclasts are noted here and there, but are nowhere abundant. A few of the marrow spaces are occupied by loose vascular granulation tissue, and the corresponding trabeculae are bordered by osteoblasts. There is, however, not sufficient evidence to warrant a diagnosis of osteitis fibrosa. Diagnosis: Rarefying Osteitis (fig. 2)."

The patient, now 8 years old, was readmitted on Oct. 5, 1931, for further study. Since his last stay in the hospital one of his sisters, aged 7, had died of meningitis, presumably tuberculous in origin. The boy at no time complained of pain, tenderness or discomfort of any kind. His activities were not limited by physical disability.

He had the typical dark complexion of his race and was alert and cheerful. His weight was 43 pounds (19.5 Kg.), and his height, 44¾ inches (102.2 cm.). The diameter of the head was 20 inches (50.8 cm.). The eyes, ears, nose and throat were normal. The teeth were poorly calcified. The lower and upper six year molars showed hypoplasia of the enamel. The temporary lower cuspid teeth were peg-shaped and anomalous in form. No masses of any kind were palpable in the neck. The diameter of the chest was 23 inches (58.42 cm.). There was angular beading at the costochondral junctions. The heart was normal.

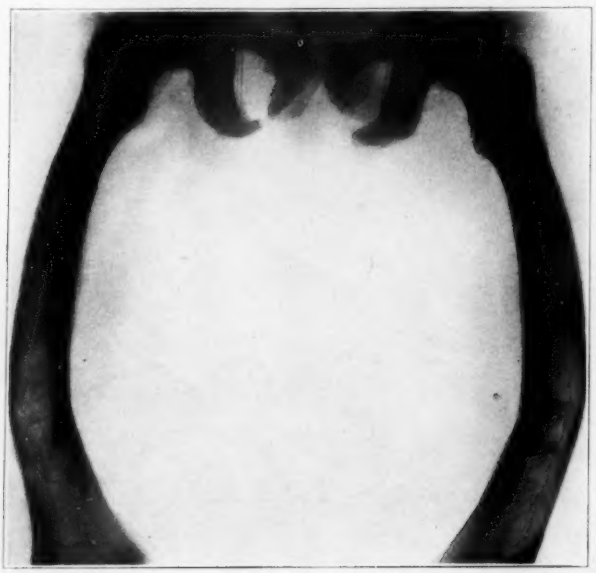

Fig. 3.—Roentgenogram of the femora, taken in 1931. Note the marked bowing with thinning of the cortex, rarefaction and vacuolization of the medulla in the distal thirds of the bones.

The pulse rate lay usually between 75 and 90. The blood pressure was 111 systolic and 78 diastolic. The lungs were clear. The abdomen was rather prominent. The hernial scar was visible, and there was no evidence of recurrence. In all other respects the abdomen was normal. The genitalia were well developed. There was no generalized lymphadenopathy. The skin was clear. Neurologic examination revealed no abnormalities. There was no hypotonia. Definite lumbar lordosis was present. Except for a waddling gait, the boy had no difficulty in walking. The genu valgum deformity was improved, with no abnormalities at the sites of operation. The bowing of the tibiae and femora was striking. There were no epiphyseal enlargements.

Roentgenographic study revealed the following: There was some thickening of the tables of the skull. The ribs showed slight deformity at the costochondral

junctions due to rickets at an earlier period. The lungs, heart and diaphragm were essentially normal. There were no apparent abnormalities in the spine. Considerable increase in the length of the long bones had occurred. Both humeri were normal. There was slight bowing of the radii and ulnae, but in other respects they were without unusual findings. The bowing of the femora was greater than in 1928, and that of the tibiae about the same. The abnormalities in the structure of the long bones of the lower extremities were essentially the same as on the previous examination (fig. 3).

*Laboratory Findings.*—The blood count showed: red blood cells, 4,100,000; hemoglobin (Sahli), 78 per cent; white blood cells, 9,800; polymorphonuclears, 58 per cent; eosinophils, 1 per cent; lymphocytes, 37 per cent, and monocytes, 4 per cent.

Chemical examination of the blood showed:

| | Oct. 9 | Oct. 20 |
|---|---|---|
| Urea | 11.8 | 13.8 |
| Creatinine | 0.5 | 0.5 |
| Uric acid | 3.5 | 3.0 |
| Sugar | 77.0 | 81.0 |
| Carbon dioxide-combining power | 48.1 | 50.0 |

| | Serum Calcium[1] | Serum Phosphorus[1] |
|---|---|---|
| Oct. 9 | 10.7 | 5.3 |
| Oct. 20 | 10.1 | 5.2 |
| Oct. 26 | 10.4 | 5.3 |

The Wasserman test of the blood was negative in both antigens; the Pirquet test was positive. Frequent examinations of the urine gave negative results.

The study of the calcium and phosphorus metabolism was carried out as follows: The patient received the following daily menu for a period of eleven days. All the food was eaten.

| Breakfast | Gm. | Lunch | Gm. | Supper | Gm. |
|---|---|---|---|---|---|
| Orange juice | 120 | Ham (no fat) | 50 | Banana | 100 |
| Sugar | 13 | Canned peas | 100 | Grade A milk | 250 |
| Grade A milk | 250 | Grade A milk | 250 | Zwieback | 20 |
| Zwieback | 20 | Zwieback | 20 | Butter | 10 |
| Butter | 10 | Butter | 10 | Corn flakes | 15 |
| Corn flakes | 15 | Baked potato | 100 | | |

The calculated composition of the diet was: carbohydrate, 163 Gm., protein, 56 Gm., and fat, 83 Gm., yielding 1,623 calories. Water was allowed as desired. A representative sample of each of the foods was analyzed quantitatively for calcium, phosphorus and nitrogen. During the last four days of the experiment quantitative determinations of calcium, phosphorus and nitrogen[2] were made on each of the twenty-four hour specimens of urine. The feces, pooled for the four day period and demarked by carmine, were similarly analyzed. The table shows the results of these examinations.

1. Serum calcium was determined by the method of Kramer, B., and Tisdall, F. F.: J. Biol. Chem. **47**:475, 1921. Serum phosphorus was determined as described by Benedict, S. R., and Theis, R. C.: J. Biol. Chem. **61**:63, 1924. Determinations of serum phosphatase were not made.

2. Calcium was determined by the method of Tisdall, F. F., and Kramer, B.: J. Biol. Chem. **48**:1, 1921. Phosphorus was determined by the method of Benedict, S. R., and Theis, R. C.: J. Biol. Chem. **61**:63, 1924. Nitrogen was determined by the Kjeldahl Method (Hawk and Bergheim: Practical Physiological Chemistry, ed. 9, Philadelphia P. Blakiston's Son & Co., 1926).

It will be readily seen that on a daily intake of 1.085 Gm. of calcium there was an average daily positive balance of only 0.062 Gm. On a daily intake of 0.848 Gm. of phosphorus there was an average daily negative balance of 0.072 Gm.

## COMMENT

The most important diagnosis to be considered is generalized osteitis fibrosa cystica. Recent work has definitely indicated a close relationship between this syndrome and hyperfunction of the parathyroid glands. Excellent bibliographies may be obtained in the articles of Barr and Bulger [3] and Hunter and Turnbull.[4] The typical clinical picture is

*Results of Determinations of Phosphorus, Calcium, and Nitrogen*

Phosphorus

| Date | Urine, Gm. | Feces, Gm. | Total Output, Gm. | Intake, Gm. | Balance, Gm. |
|---|---|---|---|---|---|
| Oct. 23, 1931 | 0.457 | ..... | ..... | 0.848 | ..... |
| Oct. 24, 1931 | 0.518 | ..... | ..... | 0.848 | ..... |
| Oct. 25, 1931 | 0.520 | ..... | ..... | 0.848 | ..... |
| Oct. 26, 1931 | 0.536 | ..... | ..... | 0.848 | ..... |
| Total | 2.031 | 1.650 | 3.681 | 3.392 | —0.289 |

Calcium

| Date | Urine, Gm. | Feces, Gm. | Total Output, Gm. | Intake, Gm. | Balance, Gm. |
|---|---|---|---|---|---|
| Oct. 23, 1931 | 0.183 | ..... | ..... | 1.085 | ..... |
| Oct. 24, 1931 | 0.233 | ..... | ..... | 1.085 | ..... |
| Oct. 25, 1931 | 0.226 | ..... | ..... | 1.085 | ..... |
| Oct. 26, 1931 | 0.200 | ..... | ..... | 1.085 | ..... |
| Total | 0.842 | 3.250 | 4.092 | 4.340 | +0.248 |

Nitrogen

| Date | Urine, Gm. | Feces, Gm. | Total Output, Gm. | Intake, Gm. | Balance, Gm. |
|---|---|---|---|---|---|
| Oct. 23, 1931 | 6.57 | .... | ..... | 8.96 | ..... |
| Oct. 24, 1931 | 6.57 | .... | ..... | 8.96 | ..... |
| Oct. 25, 1931 | 6.33 | .... | ..... | 8.96 | ..... |
| Oct. 26, 1931 | 6.40 | .... | ..... | 8.96 | ..... |
| Total | 25.87 | 4.55 | 30.42 | 35.84 | +5.42 |

characterized by the following features: Most of the cases reported have been in persons between the ages of 30 and 55. The condition is chronic and the lesions progressive. Owing to the basic pathologic conditions in the bones, there are diversified deformities such as bowing, decrease in stature, fractures and subluxation. The patients frequently complain bitterly of pain, and are weak and incapacitated. There is often marked hypotonia with decreased irritability of the muscles to electrical stimulation—the opposite of the changes in tetany. In the

3. Barr, D. P., and Bulger, H. A.: The Clinical Syndrome of Hyperparathyroidism, Am. J. M. Sc. **179**:449, 1930.

4. Hunter, D., and Turnbull, H.: Hyperparathyroidism; Generalized Osteitis Fibrosa (With Observations on Bones, Parathyroid Tumors, and Normal Parathyroid Glands), Brit. J. Surg. **19**:203, 1931.

majority of cases parathyroid tumors have been either preoperatively palpated or discovered at operation.

Microscopic examination of the bones reveals decalcification of the trabeculae and cortex, the presence of osteoid tissue, replacement of the marrow with fibrous tissue which extends into the widened haversian canals, and cysts, often hemorrhagic. There is elevation of the serum calcium, values as high as 23.6 mg. per hundred cubic centimeters having been reported. Although the serum phosphorus is sometimes lowered, the changes are not constant. Hunter and Turnbull [4] and Kay [5] reported an increased blood phosphatase. Studies in mineral metabolism have revealed that on a measured calcium intake the patients excrete a greater quantity of this element than do normal persons. Up to the present, observations in phosphorus metabolism have not yielded consistent results. Furthermore, in contradistinction to the normal condition, by far the major portion of the calcium is excreted in the urine, and not through the usual path of elimination, namely the feces.

By the injection of parathormone into a relatively normal adult, Aub [6] and his co-workers produced alterations in the calcium and phosphorus exchange as well as in the blood calcium and phosphorus that were almost identical with those found in cases of osteitis fibrosa cystica. By the repeated daily injection of parathormone, Jaffe, Bodansky and Blair [7] succeeded in producing characteristic lesions of this condition in the bones of guinea-pigs and dogs. Two of us [8] have been able to confirm these results in guinea-pigs. Further, surgical removal of parathyroid adenomas has brought about subsequent improvement in patients with the disease. It would appear, according to the present consensus, that osteitis fibrosa cystica is a manifestation of hyperparathyroidism.

Of all the conditions mentioned our case would seem to be most closely related to osteitis fibrosa cystica. Certainly the roentgen findings, essentially unchanged in their severity over a period of three years, would point to that diagnosis. The chronicity and the deformities are likewise consistent with this disease. Study of the mineral metabo-

5. Kay, H. D.: Plasma Phosphatase: II. The Enzyme in Disease, Particularly in Bone Disease, J. Biol. Chem. **89**:249, 1930.

6. Albright, F.; Bauer, W.; Ropes, M., and Aub, J. C.: Studies of Calcium and Phosphorus Metabolism: IV. The Effect of the Parathyroid Hormone, J. Clin. Investigation **7**:139, 1929.

7. Jaffe, H. L., and Bodansky, A.: Experimental Fibrous Osteodystrophy (Osteitis Fibrosa) in Hyperparathyroid Dogs, J. Exper. Med. **52**:669, 1930. Jaffe, H. L.; Bodansky, A., and Blair, J. E.: Fibrous Osteodystrophy (Osteitis Fibrosa) in Experimental Hyperparathyroidism of Guinea-Pigs, Arch. Path. **11**:207 (Feb.) 1931.

8. Abeloff, A. J., and Sobel, I. P.: Ergosterol in Experimental Osteitis Fibrosa, Arch. Path. **14**:471 (Oct.) 1932.

lism revealed that on a liberal calcium intake the child failed to retain sufficient calcium for his age requirements. From Sherman and Hawley's [9] figures, one would expect a normal child weighing 20 Kg. on an intake of about 1 Gm. of calcium a day to store 0.8 Gm. of calcium for the four day period. Our patient had a positive calcium balance of only 0.248 Gm. for this period—less than a third of the normal amount. Although according to these figures the child did not actually have a negative calcium balance, nevertheless, the subnormal retention, on a generous calcium intake of 1.085 Gm. a day, would point to a defect in the ability to store this mineral. A small calcium intake was purposely not chosen in this experiment, as we wished to ascertain how the child would handle a diet containing an optimal amount of this element. This information was deemed important for the future therapeutic regimen. Certainly with a calcium metabolism at this level the patient would never store up sufficient calcium for normal skeletal development.

On a phosphorus intake of 0.848 Gm. daily, there is actually a negative balance of 0.289 Gm. for the four day period.

The data thus far presented are not inconsistent with a diagnosis of osteitis fibrosa cystica. It will be observed, however, in the table that 21 per cent of the calcium excreted was in the urine and 79 per cent in the feces. These figures are well within normal limits. On the contrary, patients with osteitis fibrosa cystica usually eliminate the major portion of the calcium excreted by way of the urine. As much as 70 per cent or more of the calcium output may be eliminated through this channel. The calcium partition between urine and feces in our case is therefore the reverse of that usually found in osteitis fibrosa cystica.

One of the most frequent findings in cases of osteitis fibrosa cystica studied over extended periods is hypercalcemia and some lowering of the serum phosphorus. This is regarded as a cardinal manifestation of hyperparathyroidism. Three determinations of serum calcium made during the course of the patient's last admission to the hospital and one made three years previously all showed normal values. The serum phosphorus, determined on three different occasions during the last admission, was at the upper limit of normal. Such findings lend no support to a diagnosis of osteitis fibrosa cystica.

The hypotonia that has been reported frequently in cases of osteitis fibrosa cystica was absent in this boy. No tumor of any kind or any mass that could be construed as parathyroid enlargement was found in the neck. Microscopic examination of the bone removed at operation

9. Sherman, H. C., and Hawley, E.: Calcium and Phosphorus Metabolism in Childhood, J. Biol. Chem. **53**:375, 1922.

offered no confirmatory evidence for a diagnosis of osteitis fibrosa cystica. While there was definite rarefaction of the bony trabeculae, no osteoid tissue was visible, and the occasional small area of loose, vascular connective tissue could in no sense be considered fibrosis of the marrow. It might be objected that the section was not removed from a diseased portion of bone. However, the x-ray film reveals that the site of operation involved the most abnormal portion of the femur, namely, the distal metaphysis. It is the metaphyses that have been shown [10] to be the portions of the long bones most affected in experimental osteitis fibrosa cystica caused by injections of parathormone.

All other relevant diagnoses can be eliminated briefly. The clinical findings on the patient's first admission indicate that the child had had rickets in infancy. But the roentgenographic studies during the three years preceding the last admission, as well as the high serum phosphorus, dismiss rickets as a diagnosis. Renal rickets is excluded by the negative results of repeated examinations of the urine and of chemical examination of the blood. That the bones were not decalcified by the ingestion of acid is self-evident, and in addition the blood carbon dioxide was well within normal limits on two occasions. Osteomalacia is a condition that occurs most frequently in puberty and during pregnancy, with pain as one of the cardinal symptoms. Hypocalcemia has been reported [11] in cases carefully studied. The microscopic picture of the bone is often similar to that found in rickets. None of these findings occurred in our case.

## SUMMARY

1. A case of unusual and extensive bone rarefaction related to osteitis fibrosa cystica is reported in an 8 year old boy.

2. The blood calcium was not elevated.

3. Study of the calcium and phosphorus metabolism revealed a subnormal retention of these elements.

4. Contrary to the usual finding in osteitis fibrosa cystica, the ratio of the calcium excreted in the urine to that eliminated in the feces was normal.

10. Jaffe and Bodansky and Jaffe, Bodansky and Blair (footnote 7). Abeloff and Sobel (footnote 8).

11. Miles, L. M., and Feng, G. T.: Calcium and Phosphorus Metabolism in Osteomalacia, J. Exper. Med. **41**:137, 1925.

# SPONTANEOUS RUPTURE OF THE INTESTINE IN THE NEW-BORN INFANT

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Reports of peritonitis following perforation of the intestine in new-born infants are not infrequent in the literature. However, the following case may be of sufficient interest to warrant its recording.

The perforation sometimes has been known to occur during intra-uterine life. Skiles [1] recently reported such a case in which the distended abdomen of the infant caused dystocia, an abdominal paracentesis becoming necessary before delivery could be completed. Autopsy revealed peritonitis secondary to a perforation in the twisted loop of a volvulus of the small intestine.

I have reviewed the literature and have listed six cases besides my own in which the intestinal perforation was thought to have occurred during intra-uterine life. The following writers [2] reported one case each: Breslau, in 1863; Genersich, in 1891; Orth, Zillner, Pfaff, in 1899, and von Sury, in 1912. In addition to these, Salter [3] recently reported one instance in which the trauma that caused the intestinal rupture probably occurred at the time of an injury to the mother, incurred when she fell on her face five days before the birth of her child. The infant occupied a right occiput posterior position, thus presenting its abdomen to the force of the blow. The author stated that the first child of this same mother had died with symptoms of intestinal obstruction shortly after birth, and that again there was a history of the mother having sustained a fall shortly before the delivery of her baby.

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1. Skiles, James H.: Prenatal Rupture of Intestine with Subsequent Dystocia, J. A. M. A. **90**:1618 (May 19) 1928.

2. Breslau: Intra-Uterine Perforative Peritonitis in a Hydrocephalic Child, Monatschr. f. Geburtsh. u. Gynäk., 1863, suppl. 21, p. 141. Genersich, Anton: Peritonitis in the New Born as a Consequence of Perforation of the Ileum, Arch. f. path. Anat. **126**:483, 1891. Orth, J.: Lehrbuch der speciellen pathologischen Anatomie, Berlin, A. Hirschwald, 1899, vol. 3, p. 765. Pfaff, Ernest: Spontaneous Rupture of the Intestines in the New Born, Dissertation, Giessen, 1899. von Sury, K.: Spontaneous Rupture of the Intestines in the New Born, Vrtljachr f. gerichtl. Med. **43**:91, 1912.

3. Salter, A. E. Harrison: Congenital Rupture of the Jejunum, M. J. Australia **1**:422 (March 29) 1930.

The rupture frequently occurs during delivery. Reuss, in his text,[4] quoted Zillner's explanation of the mechanism as follows: The usual site of rupture is the colon, and most frequently its sigmoid portion, due to its long mesentery. Late in the period of gestation, the colon becomes overdistended with meconium; a loop of bowel, so filled, may become compressed between the infant's lumbar spine or pelvic brim and abdominal wall during delivery, and as the pressure on the loop is increased, rupture occurs at the summit of the loop.

Russell [5] recently reported a similar case. Laparotomy was done in his case too, and a gaping linear rent, 1 inch (2.5 cm.) long, was found on the right side of the head of the cecum. Shortly after operation, the infant died of the associated general peritonitis. In addition to the cases of prenatal rupture already mentioned, and exclusive of four cases in which rupture occurred during or subsequent to labor complicated by imperforate anus, Russell found thirteen other cases in which it seemed reasonably certain that spontaneous rupture of some part of the infant's intestinal tract occurred during birth. As to the effect of abnormal intestinal membranes, angulations, peritoneal pockets, etc., as etiologic factors, he reported that in nineteen cases exclusive of the four cases with an imperforate anus, such abnormalities were found at autopsy in only four, were definitely reported absent in ten and occasioned no note as to their presence or absence in five. Fischer [6] recently reported a similar case in which postmortem examination revealed perforated diverticula of the transverse colon, and of the descending colon—the diverticula consisting of herniations of mucosa and submucosa through gaps occurring normally in the muscular layer of the bowel.

The case reported by Somerford [7] of a child dying, after fourteen days of life, from a perforated duodenal ulcer and attendant peritonitis is illustrative of intestinal perforations and general peritonitis occurring some time in the neonatal period, but definitely after birth.

## REPORT OF CASE

R. C., aged 5 days, was admitted to the pediatric service of University of Kansas Hospital on May 15, 1931, with the story of having vomited everything since birth. The infant was a full-term, apparently normal boy, the third child of a healthy mother. The father was living but was said to be suffering with

4. Reuss: Diseases of the New Born, New York, William Wood & Company, 1929, p. 266.

5. Russell, Thomas H.: Spontaneous Rupture of the Intestine in the New Born, J. A. M. A. **90**:1431 (May 5) 1928.

6. Fischer, Alfred E.: Fetal Peritonitis, Am. J. Dis. Child. **36**:744 (Oct.) 1928.

7. Somerford, Anne E.: Perforation of Duodenal Ulcer in Child of Fourteen Days, Lancet **1**:1015 (May 10) 1930.

"Bright's disease." The mother's labor was severe, with onset of pains at 8 a. m., rupture of the membranes at 10:30 p. m. and a spontaneous, rather precipitous delivery of the infant at 10:35 p. m. The child weighed 8 pounds (3,600 Gm.); he was put to the breast from twenty to twenty-four hours after birth and nursed well. Vomiting began thirty-six hours after birth. He was crying and fretful all that day. The next day the abdomen was bloated, with the superficial veins quite dilated. He became too weak to nurse. There had been no bowel movement, and the infant was given castor oil, and also an enema through a soft rubber catheter inserted 6 inches (15.2 cm.) into the rectum. This brought a fair fecal return. Water by mouth was promptly expelled. The vomiting continued; the vomitus was greenish. There was some fever. On the fifth day, the baby had four convulsions and was brought to the hospital.

Examination revealed a pale, dehydrated, cachectic infant, weighing 6 pounds (2,700 Gm.) (a loss of 2 pounds [900 Gm.] since birth); the temperature was 103.4 F., the skin loose, dry and scaly, and the eyes sunken. The anterior fontanel was not easily palpable due to over-riding of the parietal and frontal bones. The abdomen was distended and tense, and the superficial abdominal veins were prominent. No masses were felt, and there was no visible peristalsis noted.

Examination of the blood showed erythrocytes, 5,780,000; hemoglobin, 120 per cent; leukocytes, 13,900; polymorphonuclears, 37 per cent; large monocytes, 3 per cent; large lymphocytes, 9 per cent; small lymphocytes, 49 per cent; polymorphonuclear eosinophils, 2 per cent.

Urinalysis showed: albumin, 1 plus; sugar, negative, and occasional pus cells and occasional hyaline and granular casts.

The initial impression was that the case was one of high intestinal obstruction at some point below the second portion of the duodenum, possibly a congenital atresia.

Physiologic solution of sodium chloride and Ringer's solution were administered subcutaneously in an effort to restore body fluids and salts before operating. Intravenous administration proved impossible, due to collapsed and fragile-walled veins. The temperature fell to 99.4 F. before operation.

Laparotomy [8] was done on the afternoon of the infant's sixth day of life. A generalized peritonitis was found secondary to two perforations in the ascending colon, each about 1 cm. in diameter. No mechanical or infectious cause for these perforations was found. The perforations were sutured and the abdominal wound closed with drains in place. The temperature rose to 105 F. after the operation, the infant's condition grew rapidly worse. Hypodermoclyses of saline and inhalations of oxygen were given, but death occurred twenty-four hours after the operation.

At autopsy [9] the following essential findings were noted: There was a fibrinous exudate over the surface of the intestine, most marked over the transverse colon and in the lower abdominal region. The descending colon from the splenic to sigmoid flexures was tremendously dilated. The transverse colon was also dilated. The region of the cecum showed a hemorrhagic area on the surface of the intestine, and a peculiar fibrous band was present in its mesentery. At the hepatic flexure were signs of sutures placed two days previously in sewing up the lacerations. The peritonitis was most marked here. The entire

8. The operation was performed by Dr. T. G. Orr of the Department of Surgery.

9. Dr. H. R. Wahl and Dr. T. J. Sims of the Department of Pathology performed the postmortem examination.

intestinal wall was inflamed in this area, and it was impossible to determine much as to the etiology of the perforations. The small intestines were matted with fibrinous exudate. The interior of the intestine at the site of the two perforations was somewhat red and hemorrhagic. The exterior showed peritonitis covering the serosa of the bowel. No other abnormalities were found. No additional information as to the etiology could be obtained from the microscopic study.

The cause of the perforations could not be definitely stated on the basis of evidence obtained in the postmortem examination. Because of the onset of symptoms so soon after birth and because no other explanation could be obtained from the postmortem examination, it would seem that this case is one of spontaneous intestinal rupture during birth due to pressure on a constricted or twisted overdistended loop.

## SUMMARY

It is noteworthy that spontaneous intestinal rupture in the new-born infant, although a rather unusual occurrence, is reported at least twenty-nine times in the literature. Abnormalities of the intestinal tract, peritoneal bands and pockets, ulcerations of the bowels, etc., acting as etiologic factors in the mechanism of the perforation, occur in less than one third of the cases. There is no satisfactory treatment for the condition, and prognosis is uniformly fatal.

# OCCLUSION OF THE CENTRAL RETINAL ARTERY IN A GIRL AGED NINE YEARS

## WITH RECOVERY OF SERVICEABLE VISION AFTER OPERATION

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Sudden blindness due to occlusion of the central retinal artery is a rare condition in childhood, and one which is generally attended by a poor prognosis as to the restoration of serviceable vision. The following case is presented because of its rarity and the beneficial results obtained by operation.

### REPORT OF CASE

*History.*—Edith R., 9 years of age, felt well on arising on the morning of March 27, 1931, but within an hour or two complained of the sudden loss of vision in the right eye. There were no premonitory symptoms. The family history was irrelevant. The patient had been in good health, except for attacks of measles at 4 years, whooping cough at 7 years and pyuria at 8 years of age.

*Examination.*—Physical examination made by one of us (M. B. G.) at 9 a. m., one hour after the onset, revealed a well developed and nourished girl of normal intelligence. The throat was not congested; the tonsils were neither hypertrophied nor diseased; there were no carious teeth, and the temperature was 98.2 F. There were no pathologic findings on physical or fluoroscopic examination of the lungs. The heart sounds were regular and forceful, with some impurity of the first sound but no actual murmur. Cardiac enlargement was not noted on either physical or fluoroscopic investigation. The pulse was regular and of good quality. The abdomen was flaccid, and did not show masses or points of tenderness; the liver and spleen were not palpable. The blood pressure was 100 systolic and 60 diastolic. Urinalysis gave negative results.

Examination of the eyes showed a dilatation of the right eye and loss of vision, except for perception of light and hand movements close to the eye. The fundus showed edema of the retina, a cherry red spot in the macula and thinning of the arteries in the upper field. The left eye was apparently normal.

A diagnosis of occlusion of the central retinal artery of unknown etiology was made, and the father was advised to consult an ophthalmologist.

An examination made by Dr. Gresser at 8 o'clock that evening revealed that the left eye was essentially normal, with normal acuity. The pupil of the right eye was fairly well dilated, but reacted to direct and consensual stimulation. The right nerve head was slightly edematous and paler than the left. The arterial system was hardly distinguishable, except that the main branches were visible but greatly narrowed. The macula possessed the typical cherry red spot surrounded

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by a grayish halo. The temporal visual field was entirely obliterated. Central vision was absent; however, light and hand movements were discernible in the nasal visual field.

A diagnosis of occlusion of the central retinal artery was made. In view of the length of time (twelve hours) that had elapsed since the onset of the complaint without improvement, immediate paracentesis of the anterior chamber was advised. The child was removed to the United Israel Zion Hospital, and operation was performed within an hour.

During the patient's stay in the hospital, a thorough investigation of all possible etiologic sources proved futile. Serologic studies, the Wassermann test, the Mantoux test and urinalysis gave negative results. Roentgenographic studies of the skull, sinuses, teeth, heart and lungs likewise were of no aid. An electrocardiographic study made by Dr. Benjamin Siegel showed a normal tracing. Dr. Siegel reported that the electrocardiogram was normal in every respect except for the following details, neither of which had any pathologic significance: (1) inverted P waves in the third lead and (2) occasional diphasic T waves in the third lead.

*Postoperative Course.*—The girl enjoyed good health until July 10 ,when chorea involving the left arm and hand and the face developed. At that time the heart action showed a good myocardial tone; there were no murmurs. The blood pressure was 100 systolic and 70 diastolic. The patient was put to bed for four weeks, and medication with phenobarbital was given. When last seen (on November 28), she was found to have a forceful heart with good myocardial tone and no murmurs. Nothing abnormal was noted on general examination.

Eight hours after operation the visual acuity was 4/200. At the end of five weeks, the acuity was 16/70, the perimetric fields showed a gross (concentric) loss of approximately 20 per cent and the retinal edema had disappeared entirely. The macula appeared slightly speckled, and the nerve head yellowish though regular in shape and outline. The arterial tree of the right eye showed a decrease in caliber in comparison with that of the left eye; however, no individual branches were found fibrosed or altered.

When the last examination was made, on May 29, the right eye was improved, by a lens, to 15/50. The optic disk was paler than the left. The retinal arteries appeared normal, and except for a slight stippling in the macular areas, no evidence of the previous insult was observed. The vision of the left eye was normal, and the interior part of the eye showed no abnormalities.

The first recorded case of occlusion of the central retinal artery is accredited to Jaeger,[1] but a diagnosis on the basis of the ophthalmologic findings was first made by von Graefe,[2] in 1859, in a case of sudden blindness and confirmed by postmortem examination eighteen months later. Since then Schobl,[3] Kober[4] and Stephenson[5] have col-

1. Jaeger, E.: Ueber die sichtbare Blutbewegung in menschlichen Auge, Wien. med. Wchnschr. **3**:5, 1854.

2. von Graefe, A.: Ueber Embolie der centralis retinae arteria, Arch. f. Ophth. (Abt. 1) **5**:136, 1859; Ischemia retinae, ibid. (Abt. 1) **8**:143, 1861.

3. Schobl, J.: Diseases of the Retina, in Norris, W. F., and Oliver, C. A.: System of Diseases of the Eye, Philadelphia, J. B. Lippincott Company, 1898, vol. 3, p. 436.

4. Kober, P.: Beitr. z. Augenh. **85**:405, 1913.

5. Stephenson, S.: Embolism of Central Artery in a Girl Aged 11¾ Years, Ophthalmoscope **9**:495, 1911.

lected one hundred and fourteen reports of this condition in patients above 16 years of age. We have been able to find only twenty-one cases in children, ranging in age from 20 months to 15 years, with a greater incidence in the upper age levels.

Occlusion of the central retinal artery may be produced by: (1) embolism, (2) thrombosis, (3) endarteritis, (4) spasm, (5) compression of the artery within the trunk of the optic nerve consequent on hemorrhage or an inflammatory process in the later or external pressure from a tumor, (6) a break in the continuity of the artery with laceration of the optic nerve at a point anterior to the porus opticus; this type of injury is frequently met with in fracture of the frontal region of the skull, and (7) air emboli. There is a difference of opinion as to whether the local conditions are due to primary local disease or to constitutional disorders.

In adults, the condition has been associated with general arteriosclerosis, apoplexy, nephritis and syphilis.[6] In children the reported cases may be classified according to the four following groups:

1. With an accompanying cardiac disease.

The simultaneous occurrence of sudden blindness, the typical ophthalmologic picture and the presence of a cardiac lesion fulfil two requisites of Harm's triad [7] for a diagnosis of embolism of the central retinal artery, namely: (1) proof of lodgment of a plug in a lumen previously free, (2) the finding of the source of the embolus and (3) absence of primary disease of the arterial wall or signs of a thrombus. Instances of this type with or without coincidental acute infection have been reported by Goldzieher,[8] Gruening,[9] Duane,[10] Rogers,[11] Stephenson [12] and Beretervide and Pozzo.[13]

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6. (*a*) Kober (footnote 4). (*b*) Fischer, quoted by Wood, C.: American Encyclopedia and Dictionary of Ophthalmology, Chicago, Cleveland Press, 1915, vol. 6, p. 4287.

7. Harms, C.: Ueber doppelseitige Erblindungen bziehungsweise Sehnstörungen durch plötzlichen, gleichzeitigen oder ungleichzeitigen Verschluss beider Zentralarterien der Netzhaut, Arch. f. Ophth. **84**:101, 1913.

8. Goldzieher, W.: Bilateral Embolie der Arteria centralis retinalis, Ungar. med. Presse, 1900, no. 20; translated, Arch. f. Augenh. **84**:145, 1913.

9. Gruening, E.: Embolism of the Central Retinal Artery in a Boy 8 Years Old, Tr. Am. Ophth. Soc. **12**:978, 1909.

10. Duane, A., in discussion of Gruening (footnote 9).

11. Rogers, W. K., in discussion of Gruening (footnote 9).

12. Stephenson, S.: Rep. Soc. Dis. Child. **61**:46, 1905.

13. Beretervide, E., and Pozzo, F.: Embolism of Central Retinal Artery in the Course of Chickenpox in a Girl of 10 Years with Mitral Insufficiency, Semana méd. **2**:1662, 1925.

2. During the course of acute infections (without cardiac involvement).

The condition has been noted in measles (Weigelin [14]), acute tonsillitis (von Graefe,[15]) chorea (Swanzy,[16] Benson [17] and Thomas,[18]), pneumonia (Karbe [19]) and "acute infections" (Leber [20]). Despite the absence of signs or symptoms of cardiac involvement, the majority of the observers have felt that the occlusion was due to an embolus. This was proved by autopsy in Karbe's case.[19]

3. Following cerebral injury.

This was the cause of the occlusion in the cases reported by Guthrie and Mayou,[21] Guthrie and Batten,[22] Jackson,[23] Elschnig [24] and Gowers.[25]

4. Without apparent etiology.

Etiologic causes were not apparent in the patients of von Graefe [15] and Werner,[26] Breiger [27] reported a case occurring in a 20 months old infant following vaccination; however, he felt that there was no relationship between the two conditions.

The prognosis for the complete return of vision is unfavorable. Partial restoration may ensue when the clot is loosened and broken up, and it passes into a smaller arteriole, or, in rare instances, when collateral circulation is established. Occlusion due to spasm is generally transitory, but repeated attacks may result in permanent blindness. Bilateral involvement is more serious than unilateral. There is always the possibility of recurrence in the same or in the other eye as long as the causative factor is present.

Dilatation of the arterioles by amyl nitrate, absorption of the clot by potassium iodide, dehydration by potassium and sodium tartrate, U. S. P. (Rochelle salts) and massage of the eyeball have been employed

14. Weigelin, S.: Erblindung nach Masern durch Verschluss beider Zentralarterien, Klin. Monatsbl. f. Augenh. **71**:692, 1923.

15. von Graefe, A.: Ueber Neuroretinitis und gewisse Fälle fulminanter Erblindung, Arch. f. Ophth. **12**:141, 1866.

16. Swanzy, H. R.: A Case of Sudden Amaurosis Associated with Chorea, Ophth. Hosp. Rep., London **8**:181, 1874.

17. Benson, quoted by Wood (footnote 6 b).

18. Thomas, quoted by Wood (footnote 6 b).

19. Karbe, M.: Ein histologisch untersuchter Fall von frischer Embolie der Arteria centralis retinae im Kindesalter, Arch. f. Augenh. **94**:190, 1924.

20. Leber, T.: Die Krankheiten der Netzhaut, in Graefe-Saemich: Handbuch der gesamte Augenheilkunde, Leipzig, W. Engelmann, 1918, vol. 7, p. 347.

21. Guthrie, L. G., and Mayou, S.: Case of Obstruction to the Left Carotid and Central Arteries, Tr. Ophth. Soc. U. Kingdom **28**:104, 1908.

22. Guthrie, L. G., and Batten, A. E.: Tr. Clin. Soc., 1903, p. 52.

23. Jackson, H.: London Hosp. Rep., 1864, vol. 1.

24. Elschnig, A.: Arch. f. Augenh. **24**:65, 1892.

25. Gowers, W. R.: Lancet **2**:794, 1875.

26. Werner: Tr. Ophth. Soc. U. Kingdom **33**:9, 1913.

27. Breiger, E.: Amaurosis fulminans im Kindesalter, Ztschr. f. Augenh. **58**: 407, 1925.

with variable results. The operations that have been suggested are paracentesis of the anterior chamber, iridectomy and sclerotomy.[28] In the first method, the drawing off of the aqueous results in the sudden diminution of intra-ocular tension, which causes the blood to flow into the eye in increased quantity and forces the clot forward if it is not too firmly fixed. Schobl,[3] Wood [6b] and others feel that operative procedures are of little value.

Occlusion of the central retinal artery is to be differentiated from other causes of sudden blindness in children, such as detachment of the retina or retrobulbar neuritis during the course of pertussis, in vitreous hemorrhage, acute glaucoma, trauma and hysteria. The ophthalmologic picture in these conditions differ from that noted in occlusion of the central retinal artery. The appearance of the fundus in amaurotic familial idiocy is similar to that in occlusion of the central retinal artery, but in the former condition there is a history of a slowly progressive bilateral loss of vision in a mentally retarded infant.

## SUMMARY AND CONCLUSIONS

An attack of sudden unilateral blindness in a previously healthy girl 9 years of age is attributed to occlusion of the central retinal artery. The diagnosis is based on the symptomatology and the typical ophthalmologic picture. Endarteritis and local spasm are excluded by the appearance of the arteries, the absence of premonitory symptoms and the persistence and progression of the blindness.

No assignable cause for the occlusion was disclosed by repeated physical and laboratory examinations.

The subsequent attack of chorea may be indicative of a "rheumatic" basis but may be unrelated.

The recovery of serviceable vision may be due in a large measure to the operative procedure employed.

A review of the literature indicates that occlusion of the central retinal artery is a rare condition, especially in children. It has been found to occur in the presence of cardiac lesion, acute infection, chorea, rheumatism, cerebral injury and with an unexplained etiologic basis.

Complete or partial permanent loss of vision is usually the result of such accidents in spite of medical and surgical treatment.

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28. Wood (footnote 6 *b*). Fuchs, E.: Text Book of Ophthalmology, translated by Alexander Duane, ed. 7, Philadelphia, J. B. Lippincott Company, 1923, p. 732.

# Progress in Pediatrics

## LEUKOPENIC MYELOID LEUKEMIA ASSOCIATED WITH ARTHRITIS

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Arthritis has rarely been described in association with any form of leukemia. The following case is interesting because of the unusual clinical picture in a 3 year old child who was studied over a period of nine months.

The white cells in the early stage of the disease showed a moderate increase in numbers, to be supplanted later by a marked leukopenia. Immature myeloid cells were identified in the blood smear. Biopsy of a lymph node revealed infiltration with cells of the myeloid series. A severe anemia coexisted with the leukopenia.

At the same time arthritic manifestations and a febrile course were sufficiently pronounced to simulate rheumatic fever. The involvement of the joints, however, did not yield to the ordinary therapeutic agents and appeared to be related to the blood disorder. Roentgenograms of the osseous system revealed profound changes in the bone which were interpreted as leukemic in origin. Postmortem examination confirmed this belief.

The association of leukemia with arthritis together with the roentgenographic alterations in the bones may conceivably constitute a syndrome the ultimate etiology of which is toxic.

### REPORT OF A CASE

The following history consists of four admissions, from March 30 to Dec. 26, 1929.

*First Admission.*—I. B., a white boy, aged 3 years, was admitted to the New York Nursery and Child's Hospital on March 30, 1929. The chief complaint at this time was painful swelling of the fingers and ankles. The patient was the only child, and there was no history of syphilis or tuberculosis. His birth history was normal, and he weighed 7½ pounds (3.4 Kg.) at the time of delivery. He had frequent attacks of nasopharyngitis, and in September, 1928, tonsillectomy was performed. Four months prior to admission, pain and swelling of both ankles developed and the patient was unable to walk. Two months later, the fingers were similarly affected. During this period the temperature was continuously elevated.

Examination showed a well nourished boy, pale but not acutely ill. The head presented no abnormalities of contour, and the eyes and nose were normal. The

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fauces were clear, but the mucous membranes were pale. The heart and lungs were normal. The lower border of the liver was palpated about 2 cm. below the costal margin. The edge of the spleen was barely palpable at the free costal margin. The lymph nodes, including the right epitrochlear, were enlarged throughout. There were swelling, redness and tenderness about the proximal joint of the right middle and index fingers and about the right ankle. The joints were warm to touch.

During this admission there were periods when the patient was free from symptoms. The spleen and liver, however, continued to increase in size; the lymph nodes became firmer and larger. An ecchymotic spot the size of a silver dollar appeared on the back. Petechiae were scattered on the body, especially over the lower part of the neck and upper part of the chest. At times the patient complained of pain in the right elbow and shoulder, but there were no objective signs of local involvement. The maximum temperature by rectum was 102 F. In an endeavor to discover a possible source of infection, roentgenograms were made of the accessory nasal sinuses. Haziness of the ethmoids was the only abnormality detected.

Because of the existing anemia, the child was given two transfusions. Following this procedure the blood picture improved, the inflammation about the joints subsided and the spleen decreased in size. The tourniquet test for capillary resistance which had been positive became negative.

The blood counts during this admission are recorded in table 1. The patient was discharged on May 1, 1929.

*Second Admission.*—The patient was readmitted on May 27. One week after the previous discharge from the hospital he complained of pain in the left elbow and later in the right knee. The symptoms in the joints were so severe that he was treated in the outpatient department for rheumatic fever. On admission at this time, the right knee was swollen and exquisitely tender. The cervical lymph nodes were especially enlarged. A soft systolic murmur was heard over the apex of the heart. The edge of the liver was palpable at the costal margin, and the spleen extended 4 fingerbreadths below the costal margin. During the patient's stay in the hospital, swelling and tenderness appeared about the following joints: the right fifth metacarpophalangeal joint, the proximal interphalangeal joints of the fourth fingers of both hands, both elbows, the left ankle and the left knee. The liver increased in size and the splenic border was felt at the level of the umbilicus. The lymph nodes were markedly enlarged throughout, particularly in the cervical region. The temperature during this period ranged between 99 and 103 F. The blood (table 2) presented evidences of a moderate secondary anemia. The white cells were moderately increased in number, and the smear showed early cells of the myeloid series in greater percentage than on the first admission.

Salicylates in large doses were administered to the patient without relief of the arthritis. The inflammatory reaction about the joints gradually subsided without any specific therapy, and the general condition of the patient improved definitely after blood transfusion.

On July 19, a lymph node was excised from the right inguinal region for biopsy. On section the excised lymph node was uniformly reddish gray and moderately firm in consistency. On microscopic examination (fig. 1) the usual structure of the node was almost completely obliterated by closely packed cells. Because of the dense staining, they appeared lymphocytic. However, higher magnification showed definitely that the cells presented myeloid characteristics. The nuclei were vesicular, nucleoli were present and the cytoplasm was pale eosinophilic in reaction. The stroma and the capillaries were obscured by infiltrating

TABLE 1.—*Observations on the Blood Following the First Admission*

| Date (1929) | Hemoglobin, per Cent | Red Cells | White Cells | Leukocytes: Neutrophilic | Leukocytes: Eosinophilic | Leukocytes: Basophilic | Leukocytes: Lymphocytes | Leukocytes: Monocytes | Immature White Cells | Platelets | Additional Data † |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 3/31 | 50 | 4,100,000 | 18,200 | 44 | 0 | 0 | 56 | 0 | | | |
| 4/ 2 | .. | ..... | 11,600 | 48 | 0 | 0 | 50 | 2 | ..... | ..... | Bleeding time, 36 min.; clotting time, 2 min. |
| 4/ 5 | 44 | 3,900,000* | 11,400 | 54 | 2 | 1 | 36 | 0 | 6 myelocytes | 70,000 | Supravital stain |
| 4/ 6 | .. | ..... | 8,200 | 26 | 0 | 2 | 60 | 10 | 1 myelocyte | ..... | |
| 4/12 | Blood transfusion | | | | | | | | | | |
| 4/14 | 60 | 3,980,000* | 10,600 | 56 | 0 | 1 | 34 | 1 | 8 myelocytes | ..... | Supravital stain |
| 4/17 | .. | ..... | ..... | .. | .. | .. | .. | .. | ..... | 240,000 | Bleeding time, 22 min.; clotting time, 2½ min. |
| 4/19 | 62 | 4,100,000 | ..... | .. | .. | .. | .. | .. | ..... | 230,000 | Fragility test: patient, beginning hemolysis with 0.5 per cent sodium chloride; complete hemolysis with 0.40 per cent sodium chloride; control range, 0.44 to 0.32 per cent sodium chloride |
| 4/24 | .. | ..... | 11,300 | 38 | 0 | 0 | 52 | 4 | 6 myelocytes | ..... | |
| 4/27 | 59 | 4,020,000 | 5,150 | 20 | 1 | 0 | 72 | 2 | 4 myelocytes | 210,000 | Bleeding time, 10 min.; clotting time, 2 min. |
| 4/29 | Blood transfusion | | | | | | | | | | |

* Less than 1 per cent reticulated and nucleated red blood cells.

† Unless otherwise designated, Wright's stain was used for blood smears.

TABLE 2.—*Observations on the Blood Following the Second Admission*

| Date (1929) | Hemoglobin, per Cent | Red Cells | White Cells | Leukocytes: Neutrophilic | Leukocytes: Eosinophilic | Leukocytes: Lymphocytes | Leukocytes: Monocytes | Immature White Cells | Platelets | Additional Data |
|---|---|---|---|---|---|---|---|---|---|---|
| 5/23* | 66 | 4,050,000† | 15,800 | 39 | 0 | 50 | 2 | 9 myelocytes | 200,000 | Bleeding time, 15 min.; clotting time, 2½ min. |
| 5/28 | 65 | 3,900,000 | 10,800 | .. | .. | .. | .. | ..... | 190,000 | Fragility test: in patient, beginning hemolysis with 0.56 per cent sodium chloride; complete hemolysis with 0.36 per cent sodium chloride; control range, from 0.46 to 0.30 per cent sodium chloride |
| 6/ 9 | 49 | 3,290,000 | 16,200 | 69 | 0 | 20 | 1 | 10 myelocytes | 170,000 | Less than 1 per cent nucleated red cells; bleeding time, 20 min.; clotting time, 2 min.; clot retraction slightly delayed |
| 6/25 | 53 | 3,860,000 | ..... | .. | .. | .. | .. | ..... | 210,000 | |
| 7/ 1 | .. | ..... | 7,900 | 42 | 0 | 44 | 1 | 7 metamyelocytes; 5 myelocytes; 1 unclassified | ..... | |
| 7/ 4 | 60 | 3,860,000† | 13,200 | 28 | 2 | 22 | 5 | 35 metamyelocytes; 8 myelocytes | ..... | Supravital stain |
| 7/12 | .. | ..... | 7,000 | 48 | 3 | 38 | 5 | 6 metamyelocytes | ..... | |
| 7/22 | 66 | 3,530,000 | 15,500 | 41 | 0 | 37 | 7 | 9 metamyelocytes; 3 myelocytes; 3 unclassified | ..... | Less than 1 per cent nucleated red cells; bleeding time, 30 min. |
| 7/23 | Blood transfusion; severe reaction | | | | | | | | | |
| 7/26 | 69 | 3,950,000 | ..... | .. | .. | .. | .. | ..... | ..... | |
| 7/27 | .. | ..... | 7,500 | 28 | 1 | 29 | 7 | 15 myelocytes; 20 metamyelocytes | ..... | Supravital stain |

* Blood count made in the outpatient department. All the others were made during the patient's stay in the hospital.
† Less than 1 per cent reticulated and nucleated red blood cells.

cells. In a few instances there was a suggestion of invasion of the capsule by scattered strands of leukemic tissue.

The patient was discharged on July 27, without involvement of the joints and with a normal temperature.

*Third Admission.*—During the two and one-half weeks following the previous discharge, the patient suffered repeated attacks of painful swelling of the joints,

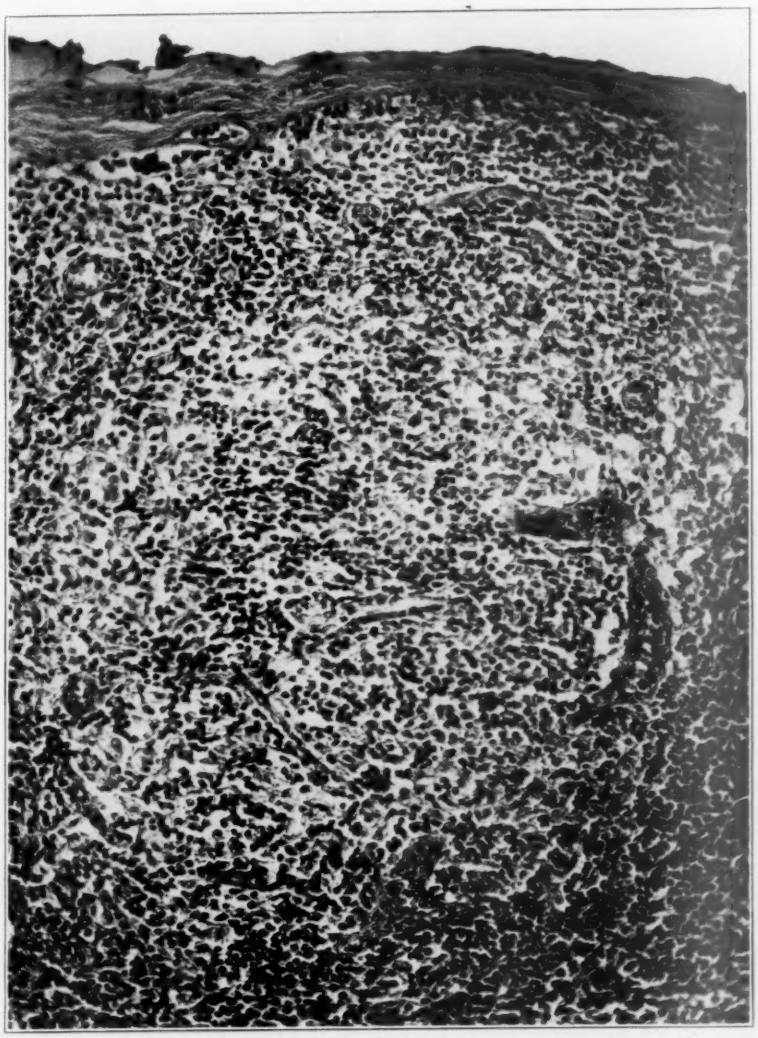

Fig. 1.—Photomicrograph of a section of a lymph node excised for biopsy; reduced from × 180. The normal markings are obliterated by closely packed leukemic cells. The finer structure of the individual cell is similar to that invading the bone marrow (fig. 5).

involving particularly the elbows and small joints of the toes and fingers. The attacks were accompanied by fever, usually lasting from three to four days. The present attack was of two days' duration. The patient was readmitted on August

TABLE 3.—*Observations on the Blood Following the Third Admission*

| Date (1929) | Hemoglobin, per Cent | Red Cells | White Cells | Leukocytes: Neutrophilic | Leukocytes: Eosinophilic | Leukocytes: Lymphocytes | Leukocytes: Monocytes | Immature White Cells | Platelets | Additional Data |
|---|---|---|---|---|---|---|---|---|---|---|
| 8/18 | .. | ..... | ..... | .. | .. | .. | .. | ..... | 180,000 | Bleeding time, 1½ hrs.; clotting time, 1 min.; clot retraction, 1 hr. |
| 8/20 | 40 | 3,460,000 | ..... | .. | .. | .. | .. | | | |
| 8/24 | .. | ..... | 7,950 | 38 | 0 | 49 | 0 | 10 metamyelocytes; 1 myelocyte | ..... | |
| 8/27 | 46 | 3,430,000 | ..... | .. | .. | .. | .. | ..... | ..... | Fragility test: in patient, beginning hemolysis with 0.68 per cent sodium chloride and complete hemolysis with 0.36 per cent sodium chloride; control range, from 0.44 to 0.32 per cent sodium chloride |
| 8/28 | Blood transfusion | | | | | | | | | |
| 8/30 | 65 | 4,200,000 | 8,350 | 30 | 0 | 61 | 5 | 4 metamyelocytes | ..... | Less than 1 per cent nucleated red cells |
| 9/ 3 | 72 | 3,840,000 | 7,300 | 10 | 2 | 78 | 4 | 6 metamyelocytes | ..... | Less than 1 per cent reticulocytes and nucleated red cells |
| 9/ 3 | Blood transfusion; mild reaction | | | | | | | | | |
| 9/ 4 | 65 | 4,200,000 | ..... | .. | .. | .. | .. | ..... | ..... | |
| 9/ 9 | 71 | 3,890,000 | 7,000 | 35 | 0 | 47 | 3 | 12 metamyelocytes; 3 myelocytes | ..... | Less than 1 per cent nucleated red cells |
| 9/16 | 62 | 3,380,000 | 5,250 | 30 | 0 | 62 | 1 | 5 metamyelocytes; 2 myelocytes | ..... | Less than 1 per cent reticulocytes |
| 9/19 | .. | ..... | ..... | .. | .. | .. | .. | ..... | ..... | Fragility test: in patient, beginning hemolysis with 0.56 per cent sodium chloride and complete hemolysis with 0.34 per cent sodium chloride; control range from 0.44 to 0.34% sodium chloride |
| 9/26 | 46 | 3,100,000 | ..... | .. | .. | .. | .. | ..... | ..... | |
| 10/ 2 | 51 | 3,340,000 | 6,150 | 50 | 0 | 39 | 1 | 10 myelocytes | 320,000 | Clot retraction, 2 hrs. |

14, with a temperature of 103 F. The right ear-drum and the throat were injected and the lymph nodes were everywhere enlarged. The liver and spleen extended 2 fingerbreadths below the free costal margin. The fingers of both hands were swollen, spindle-shaped and painful on motion. The toes, ankles, knees and elbows were similarly involved. Throughout this period of hospitalization there was marked fluctuation in the severity of involvement of the joints. The temperature, too, was elevated, ranging in the main from 101 to 102 F. Transfusions, liver extract and an iron preparation were administered to combat the anemia. At the time of discharge, October 10, the arthritis had subsided considerably and the patient was able to walk without pain. The condition of the blood was, however, essentially unchanged. There was a secondary anemia (table 3); the white cell count no longer showed a leukocytosis, but tended toward a leukopenia. Myelocytes and metamyelocytes were invariably present.

Roentgenograms taken during this and during the subsequent period in the hospital revealed pronounced changes in the bones. For the most part, these alterations consisted of atrophy and thinning of the cortex progressing to erosion, periosteal thickening at the ends of the bones and medullary rarefaction. Coarse irregular striations appearing in the medulla indicated the laying down of new bone in exhausted areas. The thinning of the cortex, the transparency and striations of the small bones of the hands, the decreased density of the marrow and the periosteal thickening of the distal end of the right ulna are shown in figure 2. Changes suggestive of osteoporosis were observed in the upper ends of both tibiae and in the distal ends of the left radius and ulna. A small area of erosion on the anterior aspect of the internal condyle of the left humerus was observed (fig. 3). The bone segments adjoining this area presented evidences of decalcification and superimposed striations.

*Fourth Admission.*—The patient was readmitted on October 30, with an interval history similar to the previous ones. Arthritis had recurred with involvement of all the fingers, the left ankle and the left knee, and it was accompanied by elevation of temperature. The condition of the patient on this admission was much worse than previously. Anemia was more pronounced, the lymph nodes were everywhere markedly enlarged and the spleen was hard and extended below the umbilicus.

During the course of his stay in the hospital, the patient showed no signs of improvement. The involvement of the joints persisted, with a temperature ranging between 101 and 105 F. A complicating otitis media appeared. In addition, the left side of the face became swollen, including in the inflammation the adjacent cervical and submaxillary lymph nodes. The mouth was difficult to open because of the swelling, and revealed large sloughing areas in the region of the molar teeth, exposing the bony surface of the mandible. Smears from the mouth were negative for Vincent's organisms. Roentgenograms showed slight localized involvement of bone. During the last week the temperature was septic, and the patient had frequent bloody stools. Epistaxis occurred for the first time. The lymph nodes and spleen were enlarged to the same degree as at the time of admission, and the edge of the liver was palpated 2 fingerbreadths below the costal margin. The arthritis subsided slightly in intensity. Death occurred on December 26.

During this admission (table 4) the red blood cells were decreased to 1,000,000 and the hemoglobin to 15 per cent. The leukopenia was extreme; few mature granulocytes were found in the blood smear, while immature cells were abundant. An autopsy was performed.

*Laboratory Data.*—The more significant blood counts are included in the tables. The Mantoux test with 2 mg. of tuberculin was negative, as were the Wassermann

Fig. 2.—Transparency and striations of the phalanges and metacarpals of the hand. Thinning of the cortex may be noted in these bones as well as in the radius. The arrow points to a zone of periosteal thickening at the distal end of the right ulna.

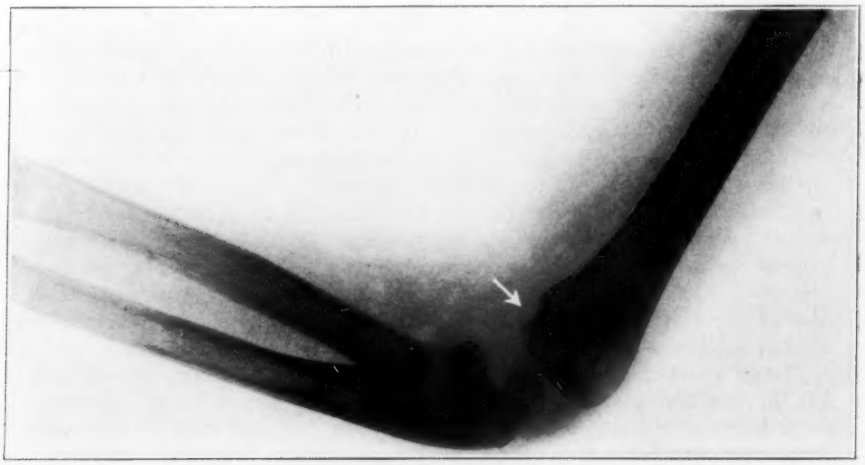

Fig. 3.—Transparency of the shafts of the radius and ulna, particularly at the distal ends. The arrow points to a small area of erosion on the internal condyle of the left humerus.

TABLE 4.—*Observations on the Blood Following the Fourth Admission*

| Date (1929) | Hemoglobin, per Cent | Red Cells | White Cells | Leukocytes: Neutrophilic | Leukocytes: Eosinophilic | Leukocytes: Lymphocytes | Leukocytes: Monocytes | Immature White Cells | Platelets | Additional Data |
|---|---|---|---|---|---|---|---|---|---|---|
| 10/31 | 30 | 2,476,000 | ..... | .. | .. | .. | .. | ..... | ..... | |
| 11/ 1 | .. | 2,450,000 | 6,000 | 5 | 1 | 53 | 4 | 19 primitive cells, probably lymphoblasts; 15 myelocytes, 3 degenerated white cells, unclassified | 130,000 | Oxidase test: positive in 18 per cent; negative in 82 per cent<br>Supravital stain; reticulocytes, 1.1 per cent; nucleated red cells, less than 1 per cent |
| 11/ 4 | .. | ..... | 2,300 | 14 | 0 | 78 | 0 | 8 myelocytes | ..... | Clot retraction, 1 hr., 15 min.; positive capillary resistance test; coagulation time, 2 min.; bleeding time, 35 min. |
| 11/ 6 | Blood transfusion | | | | | | | | | |
| 11/ 7 | .. | ..... | 1,560 | 5 | 0 | 70 | 0 | 16 myelocytes; 9 metamyelocytes | ..... | Supravital stain |
| 11/ 7 | Blood transfusion | | | | | | | | | |
| 11/ 9 | 30 | 2,350,000 | 1,000 | 22 | 0 | 77 | 0 | 1 myelocyte | ..... | |
| 11/11 | Blood transfusion | | | | | | | | | |
| 11/11 | 26 | 2,170,000 | 1,180 | 24 | 0 | 63 | 0 | 3 myelocytes; 7 metamyelocytes; 3 lymphoblasts | 120,000 | Supravital stain; no clot retraction in 22 hrs. |
| 11/15 | Blood transfusion | | | | | | | | | |
| 11/15 | 27 | 1,300,000 | 1,100 | 33 | 0 | 67 | 0 | ..... | 180,000 | |
| 11/22 | .. | ..... | 860 | 14 | 0 | 86 | 0 | ..... | ..... | |
| 11/24 | 18 | 1,370,000 | 680 | .. | .. | .. | .. | ..... | ..... | |
| 12/ 2 | 15 | 1,530,000 | ..... | .. | .. | .. | .. | ..... | ..... | |
| 12/ 4 | .. | ..... | 3,450 | 38 | 0 | 68 | 0 | 3 myelocytes; 1 metamyelocyte | ..... | |
| 12/ 8 | 15 | 1,420,000 | 4,050 | 34 | 0 | 62 | 0 | 3 myelocytes | 25,000 | |
| 12/17 | 15 | 1,000,000 | 4,150 | 23 | 0 | 72 | 0 | 3 myelocytes; 2 metamyelocytes | ..... | |
| 12/22 | .. | ..... | 6,650 | 31 | 0 | 16 | 0 | 4 lymphoblasts; 3 myeloblasts; 19 myelocytes; 27 metamyelocytes | ..... | Supravital stain |

and Widal tests of the blood. Cultures of the blood following each admission to the hospital were sterile. A test meal carried out after the first admission showed: free hydrochloric acid, 10; total acid, 40. Vincent's organisms were absent from the gums and mouth. A determination of the uric acid in the blood following the last admission showed 5.15 mg. per hundred cubic centimeters.

Fig. 4.—Photomicrograph of a section of vertebral bone marrow showing diffuse infiltration with leukemic cells; reduced from × 180.

*Necropsy.*—The body was that of a well nourished boy of 4 years. The ears showed a purulent discharge. The inner surface of the mandible was eroded.

Cavity of the Chest: The mediastinal lymph nodes were enlarged and firm. The thymus was normal grossly and weighed about 5 Gm. The pericardial cavity contained about 150 cc. of free fluid. The myocardium was pale and firm in con-

sistency. There were no valvular defects. The lungs showed a slight degree of anthracosis accentuated by the contrasting anemic appearance of the tissues.

Peritoneal Cavity: A small amount of fluid was present. The mesenteric lymph nodes were generally enlarged, firm and injected, and varied in size between

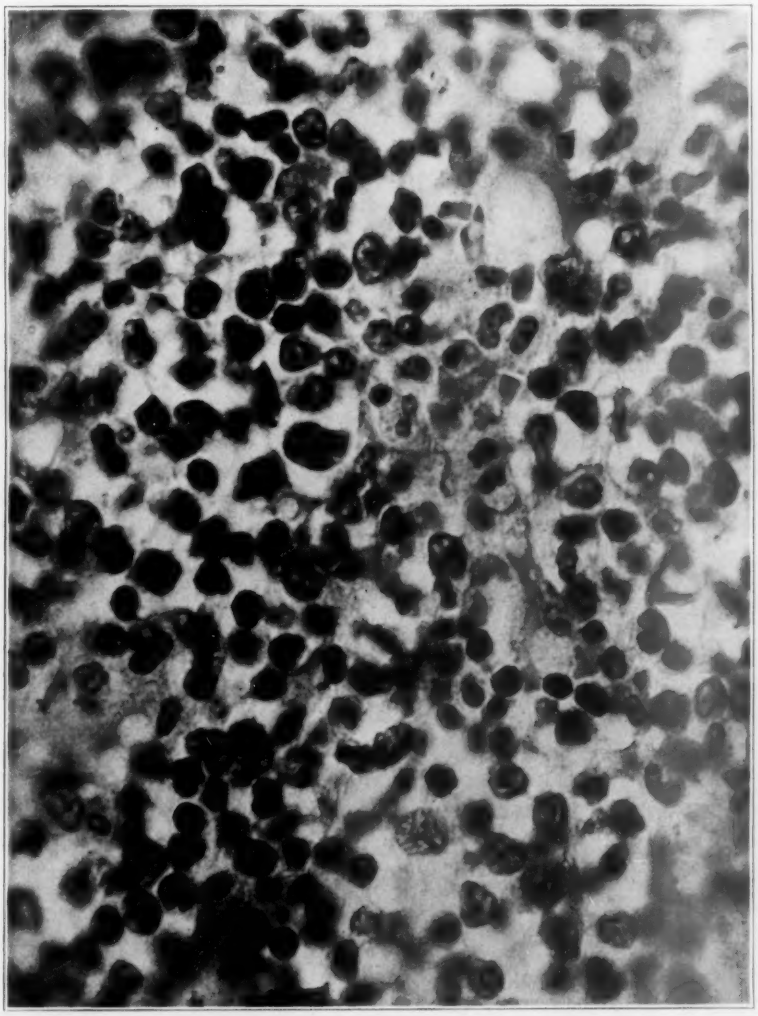

Fig. 5.—Higher magnification of a representative section of vertebral bone marrow; reduced from × 1,100. The cells are myeloid in character and similar to those infiltrating other tissues and to those observed in the biopsy of the lymph node (fig. 1).

1 and 2.5 cm. The spleen was large and weighed 396 Gm. The surface was smooth and presented several light areas, firmer in consistency than the rest of the spleen, which appeared to extend down into the tissues. The liver weighed 760 Gm., and the cut surface showed fatty infiltration. Minute petechial hemor-

rhages were present in the mucosa of the transverse colon. The lymph nodes about the pancreas were markedly injected. The capsule of the kidneys stripped with some difficulty. A few petechial hemorrhages were scattered on the surface of this organ. The normal markings were not conspicuous.

Skeletal System: The bone marrow of the vertebrae and ribs was pale. The joint cavities were not examined, owing to the limitations of the autopsy.

Microscopic Examination: The heart showed fatty degeneration. Extensive necrosis was present in the spleen, accompanied by leukemic infiltration. In the liver, there was marked fatty degeneration in the centers of the lobules with isolated accumulations of myeloid cells in the portal canals. A diffuse invasion with the same cells was noted in the mucosa of the small intestine associated with marked hyaline and fatty degeneration of the muscle wall. Aggregations of leukemic cells were evident in the kidneys. Lymph nodes from various locations showed diffuse infiltration with the same type of cell. The bone marrow of the body of a vertebra (figs. 4 and 5) and of a rib showed extensive hyperplasia. Myeloid cells almost entirely replaced the normal constituents of the bone marrow.

The individual invading cell in all of the involved organs was round or polygonal, its greater part being occupied by the nucleus. The latter was vesicular in appearance and reniform, elliptical or irregular in outline. Its chromatin was arranged in a reticulated network in whose strands were suspended several small dotlike masses, probably nucleoli. The limiting membrane of the nucleus was distinct. The cytoplasm was scanty and homogeneous, rarely granular and, with the hematoxylin-eosin stain, gave a pale eosinophilic reaction. No sharp differentiation could be made between myeloblast and early myelocyte, so that these cells were grouped together in the category of myeloid tissue. Eosinophils were occasionally visible in the bone marrow.

## SUMMARY OF THE CASE

*Clinical Features.*—From the primary appearance of pain and swelling of the ankles until the death of the patient, the duration of the illness was thirteen months. With each admission to the hospital, the chief complaint centered in the inflammatory condition about the joints. An affected joint manifested swelling, tenderness and redness and occasionally was warm to touch. Rarely was swelling unaccompanied by pain. The most frequent sites were the fingers, ankles and knees. The elbows and toes were less often affected. The extension from joint to joint as well as the appearance of the inflamed areas was typical of rheumatic infection. A febrile reaction, at times of a septic character, heralded each fresh involvement. Afebrile periods of four or five days occurred following each admission, and these were associated with subsidence of the inflammation.

Coexistent with the arthritis were the marked generalized lymphadenopathy and the enlargement of the liver and spleen. Hemorrhagic manifestations, such as petechiae and ecchymoses, occurred only rarely. Terminally, however, epistaxis and marked bleeding from the bowel took place. At this time, too, a septic process developed in the mandible.

Salicylates in large doses failed to relieve the arthritis. Transfusions invariably corrected the anemia, improved the general condition of the

patient and at times seemed more specifically to reduce the inflammation of the joints. Iron and liver had no effect in modifying the anemia.

A biopsy of an excised lymph node during the second admission cast some light on the nature of the pathologic process. The node was overrun by leukemic cells possessing the same myeloid characteristics as were found in the cells invading the tissues at autopsy.

*The Blood Picture.*—A secondary anemia was present on the first three admissions. Following the last admission, the number of erythrocytes fell to 1,000,000 and the hemoglobin to 15 per cent. Even before this stage was reached, nucleated red cells made their appearance, and polychromasia, anisocytosis and poikilocytosis were in evidence. The number of reticulated red cells was reduced below normal. The platelets, usually reduced in number, dropped to 13,000 late in the disease. The bleeding time varied between ten minutes and one and one-half hours, but was never commensurate with the diminution in the number of platelets. The clotting time was normal throughout. Clot retraction was delayed in most examinations, and in one determination it did not take place even after twenty-two hours. Increased fragility of the red cells was observed in all of the four tests made.

The white blood cells varied in number between 680 and 18,200, the latter count being observed on the first admission. In the differential count, lymphocytes appeared in increased percentage at the expense of the mature granulocytes. From the first, early cells of the myeloid series were in evidence, and ranged in maturity between the myeloblast and the metamyelocyte. In some of the smears taken on the last admission, primitive cells were observed which could not be definitely classified, but corresponded most closely to the lymphoblast. An oxidase stain of the blood on Nov. 1, 1929, showed that only 18 per cent of the cells were positive. Since the earliest cells of the myeloid series do not react to this stain, differentiation of the myeloblast from the lymphoblast by this means cannot be made. In the last stages of a severe leukemia, however, primitive cells of both lymphoid and myeloid systems may make a simultaneous appearance.

*Bone Changes.*—During the third and fourth admissions, repeated roentgenographic examinations of the long bones were made. Atrophy and thinning of the cortex were commonly found and were attributed to abnormal activity of the bone marrow. The medulla of the affected bones was mottled in some areas, as from a mild osteoporosis, and in others presented a rarefied appearance. Coarse striations observed in the rarefied areas may have represented deposits of new bone. Periosteal thickening appeared in various locations along the shafts of the long bones. Decalcification to the extent of actual erosion was noted in the distal ends of both ulnae and on the internal condyle of the left humerus.

*Diagnosis.*—The lymphadenopathy and splenomegaly with the presence of immature cells of the myeloid series in the blood were sufficient to designate the condition as leukemia. The leukopenia was unusual, but it does not necessarily mitigate against this diagnosis. The complicating arthritis with the roentgenographic evidence of bone involvement made it difficult to integrate all the features into one disease entity. The pathologic evidence of a generalized leukemic infiltration by both biopsy and postmortem examination confirmed the hypothesis of an unusual syndrome in leukemia.

In the differential diagnosis, several conditions merit consideration.

Rheumatic Fever: The inflammation of the joints was characteristic of the active phase of this disease of childhood. Early in the course of the illness, a tentative diagnosis of rheumatic fever was made despite the features pointing to a blood dyscrasia, and the child was treated on this basis. Salicylates, which act so spectacularly in relieving the symptoms in rheumatic fever, were ineffective in this case. Autopsy showed no injury to the valves of the heart, and microscopic examination of the myocardium and other tissues did not reveal the presence of the Aschoff body.

Moderate degrees of secondary anemia usually occur in rheumatic fever. The leukocyte count (Swift, Miller and Boots [1] and Wilson and Kopel [2]) is ordinarily elevated owing to an increased percentage of polymorphonuclear cells. Boyd and Lacy,[3] however, reported a case of this disease in which the blood count was at great variance with the usual one. A girl, aged 4 years, with definite rheumatic fever presented a red blood cell count as low as 1,576,000 with a hemoglobin percentage of 33. The white cells varied in number between 1,850 and 8,100, the polymorphonuclear leukocytes amounted to between 8 and 12 per cent and the small lymphocytes constituted the major percentage of cells. A few myeloblasts, myelocytes and lymphoblasts were observed in the smears. There was no lymphadenopathy or enlargement of the spleen. The blood picture in this instance may conform to a type of agranulocytosis which will be discussed later. Felty [4] collected five cases of chronic arthritis in adults of 45 years and over, in whom swellings of the joints were accompanied by generalized lymphadenopathy and sple-

1. Swift, H. F.; Miller, C. P., Jr., and Boots, R. H.: The Leucocyte Curve as an Index of the Infection in Rheumatic Fever, J. Clin. Investigation **1**:197 (Dec.) 1924.

2. Wilson, M. G., and Kopel, M.: Significance of the Leukocyte Count as an Index of Rheumatic Infection in Children, Am. J. Dis. Child. **32**:46 (July) 1926.

3. Boyd, D. H., and Lacy, G. R.: Acute Rheumatic Fever with Unusual Condition of the Blood, Am. J. Dis. Child. **37**:1337 (June) 1929.

4. Felty, A. R.: Chronic Arthritis in the Adult, Associated with Splenomegaly and Leucopenia, Bull. Johns Hopkins Hosp. **35**:16 (Jan.) 1924.

nomegaly. The white cells numbered between 1,000 and 4,200, but the differential count was normal.

Still's Disease: In 1896, Still [5] reported twelve cases in children in whom chronic fusiform enlargement of the joints was accompanied by generalized enlargement of the lymph nodes and spleen. Tenderness and redness of the joints were present only in the acute cases, and absence of pain was distinctive. As a striking feature, the lymph nodes became enlarged primarily in the region of the affected joints, and their size seemed to vary with the extent of the arthritis. Swelling of the joints was due to general thickening of the periarticular tissues rather than to any changes in the bones. Chronicity of the condition of the joints was an outstanding characteristic of the cases. The periods of pyrexia were not necessarily related to the severity of the joint involvement. Anemia was present, but was seldom pronounced. In his paper Still made no mention of the white cell count. Gross examination of the spleen and lymph nodes generally gave normal results; histologic studies were not recorded.

In the present case, the severe anemia, the leukopenia, the qualitative changes in the leukocytes, the myeloid infiltration of the tissues, the generalized lymphadenopathy unrelated to the local involvement of the joints and the febrile periods coexisting with exacerbations of inflammation serve to differentiate the condition from that described by Still.

Aplastic Anemia: The progressive anemia with the decreased tendency toward regeneration of red blood cells, the leukopenia with a diminished granulocytic response and the thrombocytopenia, all of which were pronounced following the last admission, constituted a picture analogous to that of aplastic anemia. The most significant feature of this condition, namely, the fatty or fibrous replacement of the bone marrow, was not present in the case under discussion. The absence of hemorrhage, the splenomegaly, the lymphadenopathy and the presence of considerable numbers of immature white cells also render this diagnosis untenable. The fatty bone marrow in aplastic anemia in childhood was noted in the cases collected by Herrman.[6] Baar,[7] too, emphasized this feature and cautioned against the ready acceptance of a diagnosis of aplastic anemia in childhood.

The blood picture in the early stages of leukemia often suggests aplastic anemia. Abt [8] reported a case that during life was regarded

5. Still, G. F.: On a Form of Chronic Joint Disease in Children, Med.-Chir. Tr., London **80**:47, 1896-1897.

6. Herrman, C.: Idiopathic Aplastic Anemia, Am. J. Dis. Child. **23**:484 (June) 1922.

7. Baar, H.: Ueber akute aleukozytämische Leukämie im Kindesalter, Jahrb. f. Kinderh. **104**:1, 1924.

8. Abt, I. A.: A Case of Aleukemic Leukemia with Clinical Symptoms of Aplastic Anemia, M. Clin. North America **8**:427 (Sept.) 1924.

as one of aplastic anemia, but that at postmortem examination showed leukemic infiltration of the tissues. A similar course of events was recently illustrated in another case in a boy of 5 years under observation in this hospital. In this instance, studies of the blood at the outset showed the salient features of aplastic anemia. Three months after admission, a large enough number of immature white cells made their appearance to make a diagnosis of leukemia more likely. The leukopenic stage lasted seven months and was followed by a marked elevation of the white cell count.

In the case presented in this paper the cause of the aplastic features in the blood lay, in all probability, in the invasion and crowding out of the normal hematopoietic tissues of the bone marrow by the leukemic cells. The leukopenia, however, is not wholly accounted for by this process, and possibly resulted from the lack of a chemotactic factor assumed to be present in normal bone marrow response (Sabin [9]). The anemia may be attributed in part to increased hemolysis of the red blood cells resulting from their increased fragility.

Agranulocytosis: In the course of this child's illness, leukopenia became increasingly pronounced, and on the last admission a white cell count of 680 was recorded. With these low counts, there was an accompanying reduction in the number of polymorphonuclear neutrophils. In these two respects at least, the condition of the blood resembled agranulocytosis.

Recent hematologic studies indicate that agranulocytosis is not associated solely with the clinical syndrome described by Schultz,[10] in which ulcerations in the mouth play a prominent part. Blumer [11] has pointed out that, prior to the description by Schultz, leukopenia with almost complete disappearance of the granulocytes and moderate grades of anemia had been noted in septic conditions outside of the oral cavity. Bigler and Brennemann [12] reported ten cases of sepsis in children in which the blood response was that of leukopenia, with a decrease of polymorphonuclear neutrophils below 12 per cent, severe anemia and thrombocytopenia. In only one of their cases did a necrotic lesion appear in the mouth. In some of these cases pains in the joints were present, but there was no swelling or redness. Lymphadenopathy and splenomegaly were noted at times, but were not pronounced. In this group probably falls the case of rheumatic fever of Boyd and Lacy [5]

9. Sabin, F. R.: Bone-Marrow, Physiol. Rev. **8**:191 (April) 1928.

10. Schultz, W.: Ueber eigenartige Halserkrankungen, Deutsche med. Wchnschr. **48**:1495 (Nov. 3) 1922.

11. Blumer, G.: The Agranulocytic Blood Picture in Conditions Other Than Angina, Am. J. M. Sc. **179**:11 (Jan.) 1930.

12. Bigler, J. A., and Brennemann, J.: Sepsis with Leukopenia (Agranulocytosis) in Children, Am. J. Dis. Child. **40**:515 (Sept.) 1930.

already mentioned, as well as many other infectious states with this unique blood picture. Landé [13] reported two cases, one of them in a child of 9 years in whom an agranulocytic symptom complex developed in the course of an infectious polyarthritis.

Fitz-Hugh and Krumbhaar [14] recently demonstrated that the bone marrow in agranulocytic states need not necessarily show an absence of granulocytes and of their progenitors. They described a fatal case of agranulocytic angina in an adult in whom the bone marrow showed large numbers of myeloblasts and myelocytes, while the blood count on one occasion fell to 200 cells, all of which were lymphocytes. Primitive cells of the myeloid series were found in no other organs.

While occasionally myelocytes have been noted in the blood smears in agranulocytosis, they do not appear in as great numbers and as constantly as in the case presented in this paper. The most marked leukopenia was observed simultaneously with the appearance of sloughs about the molar teeth, which would favor a diagnosis of agranulocytosis. During this period, however, the disease was in its terminal stages and the bone marrow was presumably in an exhausted state. Again, even before this complication set in, the white cell count was at one time 1,000. The striking leukopenia may be regarded, therefore, as a nonspecific reaction to an intercurrent infection which took place at the termination of leukemia. The increased fragility of the red cells and delayed clot retraction observed in the present case are not features of agranulocytosis. The lymphadenopathy and splenomegaly serve as additional distinguishing features.

Leukemia: Osseous changes occur in leukemia and vary considerably in character. It is obvious that bony alterations may be sufficiently extensive to involve the hematopoietic centers and influence the peripheral blood picture.

There is a type of bony change in which osteosclerosis is the basic pathologic process and the blood resembles myeloid leukemia. The cortex throughout the skeletal system may become thickened through the laying down of new osseous tissue. The medullary cavity is encroached on, and myeloid metaplasia of other organs such as the liver, spleen and lymph nodes takes place. Sclerosis of the osseous system may progress to the advanced forms of Albers-Schönberg's or "marble" disease and osteopetrosis as described by Karshner.[15] In these conditions, from moderate to severe grades of anemia prevail, the white cell count is low, early cells of the myeloid series may appear and the

13. Landé, K.: Der agranulocytotische Symptomenkomplex bei Infekten, Klin. Wchnschr. **9**:2015 (Oct. 25) 1930.

14. Fitz-Hugh, T., Jr., and Krumbhaar, E. B.: Myeloid Cell Hyperplasia of the Bone Marrow in Agranulocytic Angina, Am. J. M. Sc. **183**:104 (Jan.) 1932.

15. Karshner, R. G.: Osteopetrosis, Am. J. Roentgenol. **16**:405 (Nov.) 1926.

liver, spleen and lymph nodes enlarge. Into this group fall the cases of Heuck,[16] Oesterlin [17] and Mavros.[18] It is questionable whether these cases and similar ones cited in the literature represent true leukemias or whether they are reactions to the obliteration of the sites where blood is normally formed. On the basis of the latter view, Schilling [19] designated this condition as "nonleukemic myelosis." The lymph nodes and spleen are never as markedly enlarged as in the case described in this paper, the joints are not affected and the cortex of the bones is extraordinarily dense.

In case reports of leukemia, mention is made of the occurrence of pain in the bones of varying severity (Benjamin and Sluka,[20] Poynton, Thursfield and Patterson [21] and Abt [8]). Involvement of the joints, on the other hand, has rarely been observed. In a discussion of lymphatic leukemia in childhood, Strauch [22] stated that the onset may be marked by pain and swelling of the joints resembling articular rheumatism. Baar and Stransky [23] cited several instances of pains in the joints and swelling which occurred in acute leukemia and mentioned the infrequency of this association.

I have been able to collect four cases of chronic leukemia from the literature in which arthritis was a prominent feature of the disease. In none of these, however, did the white cell count reach the low levels of the present case.

In Taylor's [24] case (1926), a child, aged 2 years and 10 months, was admitted to the hospital with weakness and inability to walk of seven months' duration. The legs had been swollen, and the upper extremities from the elbows down were similarly involved. No redness was present, but the affected areas were hot and tender. The submaxillary and inguinal nodes and the spleen were enlarged. Fever developed, ecchymoses appeared and the extremities were painful on manipulation. The red cell count varied between 1,200,000 and 3,800,000; the hemoglobin between

16. Heuck, G.: Zwei Fälle von Leukämie mit eigenthümlichem Blut-respektive Knochenmarksbefund, Virchows Arch. f. path. Anat. **78**:475, 1879.

17. Oesterlin, E.: Ein Fall kombinierter Knochen-Bluterkrankung, Virchows Arch. f. path. Anat. **247**:588, 1923.

18. Mavros, A.: Aleukämische, besser "nichtleukämische," Myelose mit Osteosklerose, Folia haemat. **43**:323, 1931.

19. Schilling and Gradwohl: The Blood Picture and Its Clinical Significance, eds. 7 and 8, St. Louis, C. V. Mosby Company, 1929, p. 190.

20. Benjamin, E., and Sluka, E.: Die Leukämie im Kindesalter, Berlin, S. Karger, 1907.

21. Poynton, F. J.; Thursfield, H., and Patterson, D.: The Severe Blood Diseases of Childhood, Brit. J. Child. Dis. **19**:128, 1922.

22. Strauch, A.: Acute Lymphatic Leukemia in Early Life, Am. J. Dis. Child. **5**:43 (Jan.) 1913.

23. Baar, H., and Stransky, E.: Die klinische Hämatologie des Kindesalters, Vienna, Franz Deuticke, 1928, p. 209.

24. Taylor, H. K.: Periosteal Changes in a Case of Lymphatic Leukemia, Radiology **6**:523, 1926.

20 and 75 per cent and the leukocytes from 1,900 to 147,000. Small lymphocytes predominated in the smear, but myelocytes, myeloblasts and lymphoblasts were noted. Four aleukemic periods occurred in two months. Periosteal elevation with some productive changes was seen in the roentgenograms of the long bones, including the metacarpals and metatarsals. Postmortem examination revealed lymphatic infiltration in the spleen and lymph nodes, underneath the periosteum of the right tibia, and replacement of the bone marrow in this region. The individual joints are not described in this case report. It is assumed that they were included with the affected extremities mentioned.

In Karelitz'[25] case (1927), a boy, aged 3 years, complained of weakness, swelling of the fingers and pain in his legs. His feet and right elbow had been swollen, warm and tender for ten days before his admission to the hospital. He was pale; spindle-shaped swellings of the fingers were present; the left elbow and knees appeared larger than normal, and the lymph nodes were everywhere enlarged. The red blood cell count was 2,200,000, and the hemoglobin was 30 per cent. The leukocytes numbered 9,200, with a differential count of 24 per cent polymorphonuclears and 76 per cent small lymphocytes. Transfusion alone relieved the dactylitis and reduced the temperature. With the progress of the disease, the dactylitis and pain in the extremities recurred, the lymphadenopathy became more marked, the liver and spleen showed moderate enlargement and hemorrhages took place in the skin, eyelids and lips. The bleeding time was prolonged. Terminally the platelets numbered 18,000 and the white blood cells 33,000, with 2 per cent polymorphonuclears, 30 per cent small lymphocytes and 68 per cent myelocytes. Roentgenograms revealed periosteal elevation of the long bones of the upper and lower extremities and cortical erosion of the left radius and right ulna extending to the raised periosteum. The diagnosis of myeloid leukemia was confirmed by repeated examinations of the blood. Wassermann and tuberculin tests were negative. No postmortem examination was made.

In Hunter's[26] case (1927), a boy aged 4½ years, had a feverish attack, three months prior to admission, during which his knees and ankles became swollen and painful. Since then, pain and fever recurred about once a week. The patient was pale, the face and lower limbs were edematous and the superficial lymph nodes were slightly enlarged; the liver and spleen were within normal limits. The child died nine days after admission. The blood count one day before death was as follows: red blood cells, 550,000; hemoglobin, 12 per cent, and leukocytes, 2,200, of which 9 per cent were polymorphonuclears, 6 per cent neutrophil marrow cells, 1 per cent eosinophils and 84 per cent lymphocytes, including 48 per cent of the large variety. Postmortem examination showed infiltration of the liver, spleen, kidneys, lymph nodes and bone marrow with mononuclear cells. The prevailing cell was the lymphocyte. Roentgenographic examinations were not reported.

In Seward's[27] case (1930), a man, aged 31, was admitted to the hospital with a history of illness for seven months. During the course of this period, the complaints were weakness, anorexia, pain and swelling of both hips and shoulders and enlargement of the glands of the neck and groin. During his hospital stay of two weeks, pain recurred in the shoulders. The elbows, the knees and the region over the tarsal and phalangeal articulations were tender but not swollen.

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25. Karelitz, S.: Unusual Forms of Periosteal Elevation, Am. J. Dis. Child. **33**:394 (March) 1927.

26. Hunter, W. K.: Leukemia in Childhood, with Notes of 22 Cases, Tr. Roy. Med.-Chir. Soc. Glasgow **22**:51, 1927.

27. Seward, B. P.: Lymphatic Leucemia with Severe Pains in the Joints, M. J. & Rec. **131**:444 (May 7) 1930.

The wrists were both tender and swollen. The liver was enlarged and general lymphadenopathy was present; the spleen was not palpable. Transfusions yielded no relief. The highest temperature was 102.4 F. The lowest white cell count was 23,000; the highest noted was 64,000, and with it, the differential count showed 2 per cent neutrophils and 98 per cent lymphocytes. The red cells at this time numbered 2,006,000, the hemoglobin was 20 per cent and the platelets were 75,000. Myeloblasts were observed on one occasion in an earlier examination. The Wassermann test of the blood was negative. Roentgenographic examinations were not mentioned in this report. Postmortem examination revealed lymphocytic infiltration into the lymph nodes, liver, spleen and bone. The shoulder and elbow joints showed no evidence of hemorrhage, no erosion of the articular surfaces and no abnormality of the synovial membrane.

## COMMENT

Leukemia with a normal or low white cell count throughout its entire course, as exemplified by the case under discussion, is not unknown (Ross,[28] Bass,[29] Washburn,[30] Ramsay,[31] Hyland [32] and Kaplan [33]). The exact designation of this form of disease affords some difficulty. Virchow's original description of leukemia implies the presence not only of immature white cells but of leukocytosis. A cumbersome nomenclature has arisen from the endeavor to name the numerous deviations from the classic form of leukemia. The awkwardness of the term "aleukemic leukemia" is apparent. It has been applied to remissions in the course of a typical leukemia as well as to the condition formerly known as pseudoleukemia.

The form of pseudoleukemia in which the myeloid cells predominate is known as "aleukemic myelosis." The present case, with its extensive leukemic infiltration in the tissues and the absence of a leukocytosis in the peripheral blood, would, according to some investigators, fall into this classification. Jaffé [34] restricted this term, however, to those cases in which there is an absence of immature cells with a normal or subnormal white cell count. Pinkerton [35] took exception to such restrictions, believ-

28. Ross, A.: A Note on Three Cases of Acute Myeloid Leukemia, Lancet **2**:940 (Dec. 2) 1916.

29. Bass, M.: Leukemia in Children, Am. J. M. Sc. **162**:647 (Nov.) 1921.

30. Washburn, A. H.: Lymphatic Leukemia with Leukopenia in Young Children, Am. J. Dis. Child. **29**:631 (May) 1925.

31. Ramsay, G. W. S.: Leukemia in Infancy and Early Life, Arch. Dis. Childhood **2**:119 (April) 1927.

32. Hyland, C. M.: Lymphatic Leukemia Without Leukocytosis, Am. J. Dis. Child. **39**:59 (Jan.) 1930.

33. von Kaplan, E.: Ein Fall von aleukämischer Myelose bei einem Knaben von 7½ Jahren, Arch. f. Kinderh. **91**:283, 1930.

34. Jaffé, R. H.: Aleukemic Myelosis, Arch. Path. **3**:56 (Jan.) 1927.

35. Pinkerton, H.: Aleukemic Leukemia and Atypical Leukemoid Conditions, Arch. Path. **7**:567 (April) 1929.

ing that in "aleukemic myelosis" the blood may at some time show the qualitative changes of leukemia. King [36] would substitute the term "aleucocythemic leukemia" for those cases which show no increase of white cells. It is beyond the scope of this paper to discuss further the adequacy of the nomenclature of each type of leukemia. Contemporary literature tends to discard any sharp limitations between the subdivisions of leukemia since they merge so often with the true form of the disease. It seems that "leukopenic myeloid leukemia" is sufficiently descriptive of the blood changes in the present case.

The profound alterations in the bones of the extremities manifested by the roentgenograms are unusual features of any form of leukemia. Extensive involvement of bone resulting from invasion by leukemic tissue occurs also in chloroma, which is now regarded as a form of myelogenous leukemia. The added factor of arthritis, which was a prominent feature in the present case, is a rare accompaniment of leukemia. Unfortunately, the restrictions placed on the postmortem examination precluded inspection of the affected joints. In Seward's [27] case, in which similar arthritis was encountered, no abnormalities were observed in the affected joints at autopsy. It is conceivable that the inflammation of the joints may have been related to the extensive leukemic infiltration and resulting destruction in the ends of the bones adjoining the articulation. It is likely that the arthritis constituted an integral part of the leukemic process and was not an independent disorder. Its differentiation from rheumatic fever has already been discussed. The relief of the symptoms by blood transfusion and not by salicylates is noteworthy. One is impressed, however, in this case as well as by other blood dyscrasias occurring in childhood that the fundamental pathology is infectious in character. Steinberg [37] recently isolated an organism possessing the characteristics of Bacillus proteus from the bone marrow of a boy of 15 years with "aleukemic leukemia." He was able to reproduce the blood picture and visceral changes of the patient after the introduction of the organism into the bone marrow of rabbits.

The febrile reaction, the arthritis and the marked leukopenia paralleling the low white cell levels recorded in agranulocytosis point to an infectious etiology in the present case. The toxic factor which may have been instrumental in producing the changes remains unknown.

36. King, J. T.: Aleucocythemic Leukaemia, Bull. Johns Hopkins Hosp. **28:** 114 (March) 1917.

37. Steinberg, B.: Experimental Production of an Aleukemic Leukemic Condition, Arch. Path. **9:**1299 (June) 1930.

SUMMARY

Leukemia with a normal or subnormal white cell count throughout its course is a recognized entity.

A case is reported in a child, aged 3 years, who was observed over a period of nine months. The white cell count was usually normal or decreased, and on one occasion fell to 680 cells. Early cells of the myeloid series appeared in considerable numbers. This type of leukemia is designated as leukopenic myeloid leukemia.

A severe polyarthritis resembling rheumatic fever was associated with the blood disorder. Roentgenograms revealed periosteal thickening, cortical erosion and medullary rarefaction.

Extensive invasion of the tissues with myeloid cells was observed at postmortem examination. Leukemic infiltration into bone was marked.

Differentiation was made from rheumatic fever, Still's disease, agranulocytosis, aplastic anemia and osteosclerotic anemia.

Four other cases of leukemia associated with arthritis are reviewed.

Infection is suggested as a possible etiologic basis for this syndrome.[38]

113 East Eighty-First Street.

38. Since this paper was submitted for publication, the report of another case including autopsy has appeared in the literature which resembles in essential features the one presented (Poynton, F. J., and Lightwood, R.: Lymphatic Leukemia with Infiltration of Periosteum Simulating Acute Rheumatism, Lancet **1**:1192 [June 4] 1932).

# Pediatrics in Art

## THE INFANT BINDER

JOHN RUHRÄH, M.D.
BALTIMORE

Andrea Montegna (1431-1506), an Italian painter and engraver, made a contribution to the history of pediatrics in his excellent reproduction of the binder used since the earliest times in Italy and persisting

The Presentation of Christ in the Temple

even today. It is seen in his "Presentation of Christ in the Temple," which hangs in the Kaiser Friedrich Museum, in Berlin. Soranus and other early writers give very meticulous directions as to its application. Sometimes the binders were as long as twenty or thirty feet, and the child was encased like a mummy. This was supposed to be most important and was thought to be a preventive of bowlegs and other deformities. Few illustrations show it any better than this beautiful painting.

# Pediatric Biographies

## PEDIATRIC AND POLITICAL BROADSIDES

JOHN RUHRÄH, M.D.
BALTIMORE

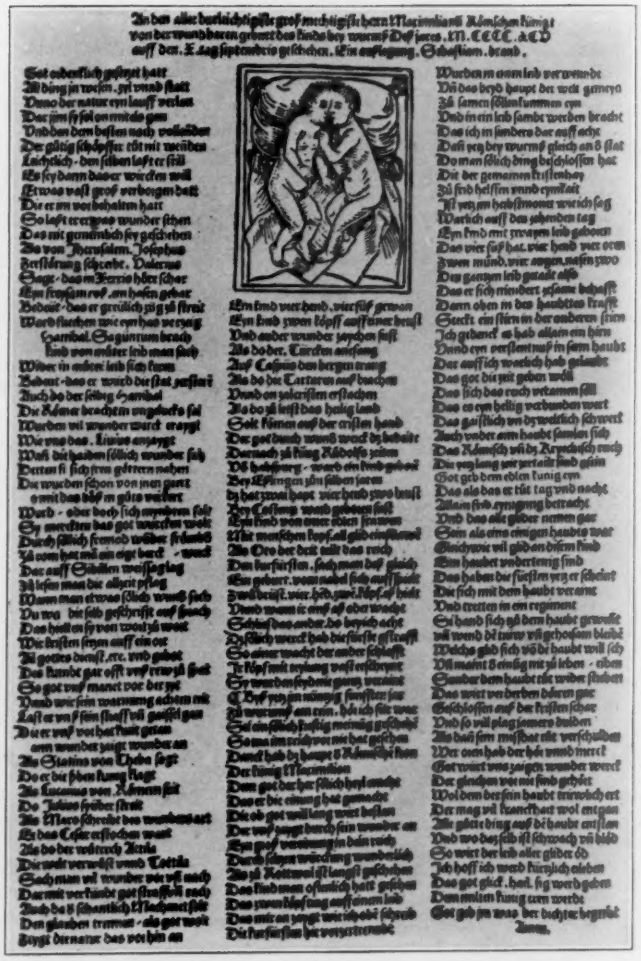
Politics, it is said, makes strange bedfellows, even in the field of pediatrics, as witness the politico-pediatric endeavors of Sebastian Brant. His history has been told by J. H. E. Hetts in "Flugblätter des Sebastian Brant," Strassburg, 1915, as to how, by using rhymed broadsides, he hoped to uphold his ruler, Maximilian. About this time there were born at Worms two children fastened together by their heads. Brant, remembering how in the past such things had been regarded as signs of importance, composed a poem trying to show that this event was a favorable omen. This was issued in 1496, four years after Columbus landed in America. The illustration gives the text, part of which may be freely rendered as follows:

> When Hannibal brought victory, a child coming from its mother's womb returned there. It meant Hannibal would destroy the city. Livius tells of many wonders which foretold disaster to the Romans. . . . And so at last God, in King Rudolph of Hapsburg's time, by wonders indicated that the Holy Land would pass from Christian hands—a child was born at Esslingen the same year and it had two heads, four hands, two breasts, and at Constance a child was born of a noble woman with a man's head and all the members. . . . When Otto the Third divided the kingdom there was born a child divided from the navel with two chests, four hands and two heads, one sleeps while the other wakes. . . . And now in the ninety-fifth year in Worms I hear there have been such a happening as man never before has seen . . . a child born with two bodies that has four feet, four hands, four ears, two mouths, four eyes, two noses and the bodies separate, but above one forehead joins with the other. I think it has but one brain and one understanding, a sign that God will give a time when the empire shall be united in holy union, the spiritual and wordly sword will come together under one head.

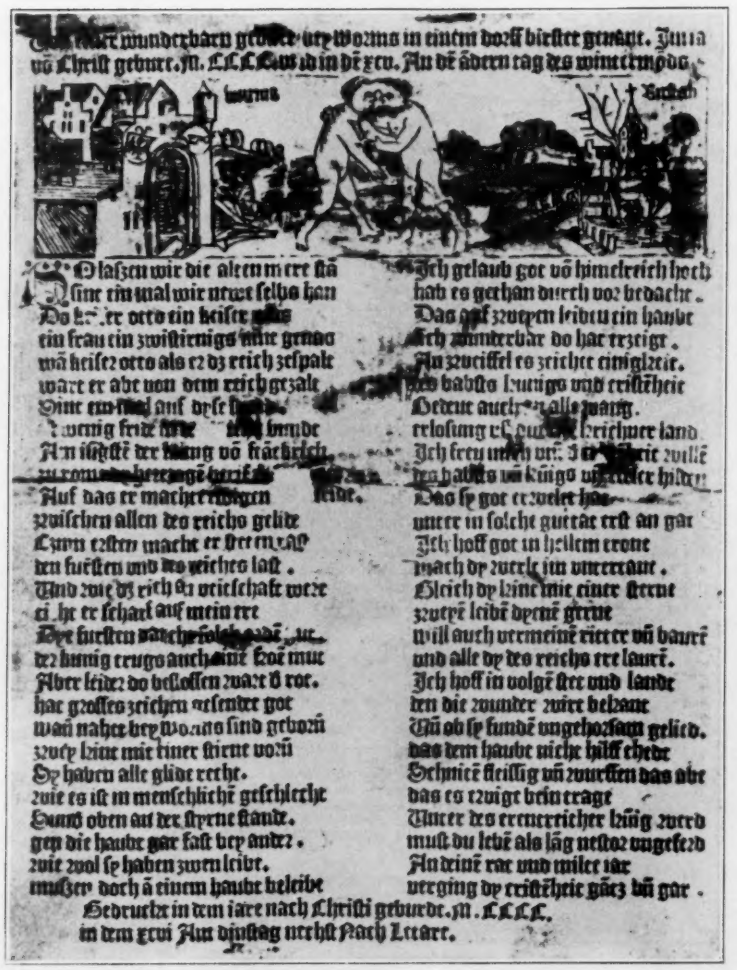
He closes with a pious wish:

> We have ears that hear, so mark, God will show us a wonder the like of which has not been heard of. He who truly honors his head may avoid much illness. All good things arise in the head and where it is weak and foolish so will all the members of the body be dull. I hope I will shortly experience that God will give luck, safety and victory.
>
> God give to the mild King, worthy of honor, the poet prizes. Amen.

Another anonymous broadside is in the Munich Library. The two children with their heads joined together are seen, and on one side is the town of Worms and on the other the Berstett churchyard. This, too,



A broadside of Sebastian Brant, dated 1496. The Worms twins. (From Holländer's "Wunder, Wundergeburt und Wundergestalt." Courtesy Ferdinand Enke, Stuttgart.)



A broadside dated 1496. The twins of Worms. (From Holländer's "Wunder, Wundergeburt und Wundergestalt." Courtesy Ferdinand Enke, Stuttgart.)

A broadside by Heinrich Vogtherrn dated 1544. The Heidelberg twins. (From Holländer's "Wunder, Wundergeburt und Wundergestalt." Courtesy Ferdinand Enke, Stuttgart.)

expresses the same idea. Brant issued other broadsides about misformed animals, including one about a pig's head with four ears. This was "Die wunderbar Sau zu Landseer," which was engraved by Dürer.

Another broadside concerning twins born at Heidelberg of the honorably married Hausfrau Katherine, was issued with the assistance of Caspar Betzler, by Heinrich Vogtherrn and was illustrated by Schleffer. This was printed by Herman Gülfferich of Frankfort-on-Main, in 1544, who also printed in the same year a poem on the care of children noted in the article on Louffenburg.

These broadsides are of interest in showing how far afield pediatric subjects may go and are unusual examples of little known pediatric poems.

# Correspondence

## "TETANISM"

Nov. 4, 1932.

*To the Editor:*—Through a reprint recently distributed by the Sandoz Chemical Works I learned of an article that appeared in the AMERICAN JOURNAL OF DISEASES OF CHILDREN by Dr. Harold T. Nesbit on "A Syndrome Occurring in the Neonatal Period Manifesting Tetany-Like Symptoms." May I call attention to the fact that this group of symptoms was described and illustrated by me under the heading of "Tetanism" as early as August, 1910, in the *Archives of Pediatrics* and subsequently in other journals, as well as in my books on pediatrics? The cyanosis and edema Dr. Nesbit refers to vary with the degree and duration of the muscular contractions, and hence do not form a constant symptom, and were not particularly emphasized in my original paper. A little study of past literature might have aided Dr. Nesbit to obtain a clearer perspective of the subject in question.

HERMAN B. SHEFFIELD, M.D., New York.

Dec. 12, 1932.

*To the Editor:*—The symptom complex as presented in Dr. H. B. Sheffield's two reprints has many characteristics common to those which I presented in my article in the August issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN (page 287). Although my instances occurred during the first few weeks of life, whereas his did not, the syndrome may be present at later periods during the first year of life. The history of each of my cases indicates that excessive crying, hypertonicity, hyperperistalsis and spasm of the extremities had existed to a varied extent since birth. Beyond the neonatal period I have a group of forty infants which more resembles the instances described by Dr. Sheffield. The majority of them have presented evidence either in the history or at the time of examination of attacks of projectile vomiting and retraction of the head. A smaller proportion has had cyanosis, edema and altered crying. It is my presumption that the accompaniment of these latter grave symptoms has often resulted in a fatal outcome, therefore accounting for their minority in the older group of infants.

I shall elaborate just a little, as the article under discussion included infants only in the first few weeks of life, whereas my older infants with this symptom complex more closely approximate those described by Dr. Sheffield. In his instances no cyanosis, edema or altered character of cry was noted. In the following manner the group under my observation resemble the cases described by Dr. Sheffield: A more or less constant muscular hypertonicity persists during the first few months of life, which is increased by handling but never interferes with feeding. Vomiting, often projectile, frequently accompanies this. My infants have, in addition, the voracious appetite, whether or not vomiting occurs, even when they are taking a considerably higher caloric intake than is necessary. The infants suffer from hyperperistalsis (or colic as Dr. Sheffield describes it). During "the acme of the spasm," extension of the arms, fingers, legs and toes, together with a fine tremor, occurs. In Dr. Sheffield's cases this did not occur (whether flexion or extension occurs, however, depends on the predominating strength of the flexor or extensor muscles). Retraction of the head and occasional strabismus

may accompany the spasm. The flexion of the elbows, the fist position of the hand and the lower extremities, "bent angularly," simulate my observations. In an untreated patient this position of the extremities is constant except when an actual spasm, as described, occurs.

Even though invaluable details regarding the history and physical findings are lacking, I do think that Dr. Sheffield's description of "Tetanism" represents the same symptom complex as the cases presented in the August issue and also the instances referred to in this letter, which I presented on Oct. 22, 1932, at the annual meeting of the Texas Pediatric Society. Dr. Sheffield implies that this condition occurs in marantic infants, whereas my patients were usually well nourished and frequently overweight, regardless of the fact that almost every conceivable formula may have been proffered in an attempt to bring relief. I can agree that a faulty chemical assimilation of some sort may be an etiologic factor, but I have not been able to demonstrate tuberculosis or syphilis as related to this condition. Like artists, most of these infants are born that way, as careful observation will note that varying symptoms of vagotonia have persisted from the first few hours of life. Often, however, the child is not seen by the pediatrician until the symptoms have become aggravated.

I shall reserve the detailed discussion of what I consider the causative factor for a paper that I hope will be accepted for publication. Suffice me to say now that a more diligent observation of the factors governing calcium metabolism during pregnancy will very likely mitigate the occurrence of this syndrome. The use of vitamin D, acid milk, calcium gluconate (Sandoz) or, in an aggravated case, parathyroid and x-rays will provide the prompt relief in an established instance. The relief following parathyroid or roentgen ray therapy is but temporary. In Dr. Sheffield's cases the gradual amelioration of the symptoms was probably brought about by the use of malt soup, which renders a more acid condition in the gastro-intestinal tract, thereby causing a greater utilization of calcium.

HAROLD T. NESBIT, M.D., Dallas, Texas.

# News and Comment

## GENERAL

**Exhibit on Diseases of Children at Milwaukee.**—The Section on Pediatrics of the American Medical Association has appointed a special committee on section exhibit to cooperate with the Committee on Scientific Exhibit in promoting an exhibit on diseases of children for the Milwaukee Session of the American Medical Association, June 12 to 16, 1933. The special committee consists of F. Thomas Mitchell, chairman, Memphis, Tenn.; Charles F. McKhann, Boston, and M. G. Peterman, Milwaukee. The closing date for applications is February 13. Application blanks for the exhibit may be obtained from members of the committee, or from the Director, Scientific Exhibit, 535 North Dearborn Street, Chicago.

**Appointments.**—Dr. C. Sáinz de los Terreros has been named titulary professor of the School of Hygiene at the National School of Health in Madrid.

Drs. Garelly, Cardenas and E. Jaso have been placed in charge of the Antituberculous Dispensary in Madrid.

**Bequests and Donations.**—St. Mary's Free Hospital for Children, New York, was given $25,000 by the will of Delancey Nicoll.

St. Louis Children's Hospital received $30,000 by the will of the late Mrs. Amanda Fox Horning.

## DEATHS

Dr. G. Racchi, physician-in-chief of the Asylum for Abandoned Infants in Naples, died at the age of 65.

## UNIVERSITY NEWS

The Boston University School of Medicine, Boston, announces the following faculty appointments: Dr. Martin J. English to professor and head of the department of pediatrics and Dr. Herman C. Petterson as associate professor of pediatrics.

## PERSONAL

Dr. B. Weill-Hallé has been promoted to the grade of Officer of the Legion of Honor.

# Abstracts from Current Literature

## Pathology, Bacteriology and Biochemistry

CULTURES OF LEUKEMIC BLOOD LEUKOCYTES. MILA PIERCE, Arch. Path. **14**:295 (Sept.) 1932.

Detailed accounts are given of the observations made during the growth of cultures of leukocytes taken from two patients with chronic myelogenous, one with chronic lymphatic, three with myeloblastic and one with acute lymphatic leukemia. The case histories are briefly sketched.

In the myeloid and myeloblastic types, myelocytes, polyblasts, fibroblast-like cells, monocytes and hemocytoblasts developed.

In the chronic lymphatic type, a few monocytes and many polyblasts and fibroblast-like cells appeared, although many of the explanted cells remained unchanged.

In the acute lymphatic type, monocytes, polyblasts, fibroblast-like cells and epithelial cells developed in large numbers as well as hemocytoblasts, morphologically identical with those found in lymph nodes and bone marrow.

The development of these hemocytoblasts from known small lymphocytes is of hematologic significance since, according to the unitarian school, in both the embryo and the adult normal body the free stem cell is a polyvalent cell capable of producing all other types of blood cells.

It is felt that the tissue culture method may prove to be of diagnostic aid in leukemias in which the "blast" forms dominate the blood picture.

LEMASTER, Evanston, Ill.

EXPERIMENTALLY INDUCED DESCENT OF THE TESTIS IN THE MACACUS MONKEY BY HORMONES FROM THE ANTERIOR PITUITARY AND PREGNANCY URINE. EARL T. ENGLE, Endocrinology **16**:513 (Sept-Oct.) 1932.

Ten immature male monkeys were subjected to injections of extracts of urine taken during pregnancy and water-soluble extracts of anterior pituitary, with the result that the testes descended into the scrotum. Under normal conditions no monkeys of similar weight in a large number under observation were found with testes in the scrotum. Coincident with this descent, the testes doubled in size and acquired a greater range of mobility, and there was a pronounced increase in the amount of interstitial tissue. In none of the animals was there a hastening of spermatogenic activity, the action of the injected substance being apparently only on the hormone-producing structures.

The significance of these findings in explaining the results of hormonal factors acting on the genital system of human fetuses is suggested. The increase in the amount of the interstitial cell mass in the testis in the eighth and ninth fetal months is similar to the experimental increase in the amount of this tissue in monkey testes after injections of pregnancy urine. And the descent of the testes into the scrotum in the experimental animals is probably due to the same factors as produce this phenomenon in the human new-born infant which derives this hormone from the maternal circulation or placenta.

The human being is the only animal in which the testes descend at birth, and significantly the human female is the only one which is known to have this gonad-activating principle in the circulation throughout the period of gestation.

JACOBSEN, Buffalo.

ON THE STIMULATION OF NEW BONE FORMATION WITH PARATHYROID EXTRACT AND IRRADIATED ERGOSTEROL. HANS SELYE, Endocrinology **16**:547 (Sept.-Oct.) 1932.

Ordinarily an overdosage of parathyroid leads to formation of osteoclasts and bone resorption. But when rats previously treated with this hormone are later subjected to overdosage over long periods the formation of osteoblasts is stimulated and the bones become denser than normal, according to these experiments. Further, when parathyroid hormone is administered in very small doses it will lead to stimulation of osteoblasts and thereby to bone apposition without previous formation of osteoclasts and fibrous transformation of the bone marrow.

A single large dose of parathyroid hormone produces within twenty hours an osteitis fibrosa, but as soon as this is healed, even as early as forty-eight hours after the injection, a very active formation of new bone appears.

While it is true that large doses of irradiated ergosterol lead to resorption of bone and small doses to increased density, these studies show that the histologic features of these bones are definitely different from those produced by parathyroid hormone.

JACOBSEN, Buffalo.

VEGETATIVE NERVOUS SYSTEM AND CALCIFICATION OF BONE IN EXPERIMENTAL RICKETS. G. GUASSARDO, Riv. di clin. pediat. **30**:737 (June) 1932.

Rats put on a diet to produce rickets show an increase in the calcium and phosphate of the bone if choline or ergotamine is given. Neither epinephrine nor atropine had any effect.

Thus stimulation of the vagus nerve (choline) or inhibition of the sympathetic nerve (ergotamine) acts to prevent rickets, while inhibition of the vagus (atropine) or stimulation of the sympathetic (epinephrine) does not prevent rickets.

HIGGINS, Boston.

METHOD FOR THE DETERMINATION OF THE MELTING POINT OF FAT. C. COCCHI, Riv. di clin. pediat. **30**:752 (June) 1932.

A small piece of the fat to be studied is placed on the side of a test tube in a water bath, the temperature of which is raised slowly (0.5 degree C. per minute). A capillary glass rod rests in the fat and extends beyond the tube; this rod is bent at a point outside the tube and so placed that gravity will cause it to rotate when the fat has melted.

HIGGINS, Boston.

THE RESISTANCE OF THE ERYTHROCYTES OF INFANTS AND OF CERTAIN MAMMALS TO THE LOWER FATTY ACIDS. V. BORRA, Jahrb. f. Kinderh. **136**:239 (Aug.) 1932.

The whole blood or washed erythrocytes of infants, goats, kids, calves, horses, steers and hogs were mixed with equal volumes of fatty acids in Ringer's solution. The lowest hemolytic concentrations of acids were found to be: butyric, 1:6,000; caproic, 1:5,100, and caprylic, 1:1,800.

CLAUSEN, Rochester, N. Y.

## Nutrition

LEMON JUICE EVAPORATED MILK IN INFANT FEEDING. OSCAR REISS, Arch. Pediat. **49**:170 (March) 1932.

The writer has made use of lemon juice evaporated milk in the feeding of both well and sick infants, and the result has been most gratifying. Gastro-intestinal upsets appeared less frequently, and satisfactory gains in weight resulted. He feels that such formulas compare favorably with fresh milk formulas as to safety, digestibility and nutritional value. Such formulas were found to be particularly useful as a complement to or a substitute for breast milk. Reiss particularly recommends this type of feeding in institutions and in the homes in which cost is an important item.

WADDELL, JR., University, Va.

A Quantitative Study of the Dietary of the Human Mother with Respect to the Nutrients Secreted into the Breast Milk. C. E. Shukers, J. G. Macy, B. Nims, E. Donelson and H. A. Hunscher, J. Nutrition **5**:127 (March) 1932.

Three housewives carrying on their usual home duties who had sustained continuous reproductive processes for a period of from four to six years were used as the subjects for the following observations. The average daily output of milk over a sixty week period was 3,134, 2,366 and 1,419 cc., respectively. The diet was liberal and composed of the foods that the women liked.

The caloric content of the breast milk in these women was equivalent to 50, 33 and 30 per cent of the total caloric intake. The variation in the caloric value of the milk was not related to the volume.

The results of the observations on the relationship of the intake of food to the production of milk indicate a need for more comprehensive observations on women and a closer scrutiny of the present empiric standards for lactation, which are based largely on experiments on mammals other than man.

The concentration of fat in breast milk resembled the caloric concentration. The highest fat concentration was achieved by the woman producing the smallest volume of milk. The milk fat secreted by these three women was equal to 74, 50 and 43 per cent of the total intake, respectively.

The protein secretion equalled 21, 15 and 12 per cent, respectively, of the total intake. The concentration of protein in the breast milk was similar for all subjects, but the milk of the smallest producer showed a 20 per cent higher value than that of the other woman.

The calcium and phosphorus values of the breast milk were fairly constant. The intake of calcium and phosphorus was in inverse relation to the volume of milk and hence to the total excretion in the breast milk. Although receiving liberal quantities of foods from which calcium and phosphorus are usually well assimilated, the women were unable to absorb or utilize calcium and phosphorus adequately while maintaining a high level of milk flow. The deficiency in the balance may have been made up by withdrawal from the natural storehouses of the body.

The data indicate, on the whole, that more satisfactory ways of inducing better digestion, absorption and assimilation of food materials taken into the body must be devised if lactation is to leave the maternal body unimpaired.

Munns, Winnetka, Ill.

The Iron Requirement of the Pre-School Child. Jane M. Leichsenrig and Iva Hansen Flor, J. Nutrition **5**:141 (March) 1932.

Studies were conducted on the iron balance of four healthy children. The retention of iron at two levels of intake was studied. Analysis of the various foods included in the diet revealed that the iron content was 35 and 24 per cent less than the calculated amount. These figures indicate that the iron content of foods may show considerable variation from the commonly used figures.

Children receiving a high proportion of iron retained relatively more of the mineral. Thus on a diet containing 3.25 mg. of iron, an average of 1.2 mg. was retained against 3.2 mg. when the intake was 6.5 mg. Apparently, the maintenance requirement of a child is similar to that of an adult.

This study indicates that the requirement of iron for growth is approximately 0.2 mg. per kilogram.

Because of the evident variation of actual iron content of foods as compared to the calculated content, the authors suggest that a 50 per cent margin of safety be allowed over the total requirement of 0.32 mg. per kilogram.

Munns, Winnetka, Ill.

THE SPECIFIC EFFECT OF VITAMIN B ON GROWTH. BARNETT SURE, M. C. KIK and M. E. SMITH, J. Nutrition **5**:155 (March) 1932.

Working with nonlactating, weaned white rats, the authors concluded that vitamin B produces growth in two ways: 1. It possesses the physiologic function of stimulating growth, per se, unrelated to the intake of food. 2. It produces growth by increasing the plane of nutrition through a stimulation of the appetite.

MUNNS, Winnetka, Ill.

FAILURE TO PRODUCE EXPERIMENTAL DENTAL CARIES IN THE WHITE RAT WITH HIGH CARBOHYDRATE DIET AND BACILLUS ACIDOPHILUS OR WITH VITAMIN D DEFICIENCY. C. A. LILLY, J. Nutrition **5**:175 (March) 1932.

Dental caries did not develop in white rats fed a normal diet for one year. Rats fed for one year a diet of which 53 per cent was saccharose, but otherwise normal, had no dental caries. Rats fed a diet about the same as the latter and given triweekly oral inoculations of a pure culture of Bacillus acidophilus had no dental caries. Florid rickets with extreme deformities of the bones and joints but no dental caries developed in white rats that survived on a rachitogenic diet for long periods, from eight to twelve months.

MUNNS, Winnetka, Ill.

CHARACTERIZATION OF VITAMIN A: I. SPECTROSCOPIC EVIDENCE. I. M. HEILBRON and R. A. MORTON, J. Soc. Chem. Ind. **50**:183-4T, 1931.

By examining spectroscopically many liver oils in varying degrees of freshness and also by determining the absorption bands in the antimony trichloride color test, the following criteria for vitamin A are postulated: a colorless or almost colorless substance, exhibiting an absorption band without fine structure and absorbing maximally at from 320 to 330 millimicrons, and giving with antimony trichloride a sharp absorption band at 583 millimicrons, the intensity of the absorption of both bands being approximately the same for equal weight of vitamin. These criteria were approximately the same for equal weights of vitamin. The criteria were applied to a reduction product of carotene, with partial success.

CHARACTERIZATION OF VITAMIN A: II. BIOLOGIC EXPERIMENTS. B. AHMAD and J. C. DRUMMOND, J. Soc. Chem. Ind., **50**:184-6T, 1931.

Absorption of carotene fed to rats rendered vitamin-A-free is more nearly complete when the basal diet contains 10 per cent fat than when it is fat-free. A preliminary report of experiments performed to follow the fate of absorbed carotene and of reduced carotene is given.

KUGELMASS, New York.

CHRONIC VITAMIN B DEFICIENCY: A CLINICAL STUDY. HENRY E. MARKS, M. J. & Rec. **135**:231 (March 2) 1932.

Chronic deficiency in vitamin B is of fairly frequent occurrence in medical practice. The symptoms of deficiency are: (1) a tendency to the development of chronic gastro-intestinal disorders (anorexia, indigestion, constipation and colitis) and the sequelae of such disorders (headache, biliousness, eruption of the skin, etc.); (2) malnutrition and impaired assimilation of food, and (3) impairment of strength, vigor and resistance. Cereal germ is an efficient source of vitamin B for use in the treatment of such deficiencies.

WILLIAMSON, New Orleans.

A POSSIBLE CORRELATION BETWEEN VITAMIN A DEFICIENCIES AND RESPIRATORY DISEASES. E. J. QUINN, M. J. & Rec. **135**:237 (March 2) 1932.

Vitamin A has a definite rôle in the prevention of colds and diseases of the respiratory tract. This vitamin, by increasing the body's resistance and by combating infection, has a favorable effect in the prevention and cure of such afflictions.

Sherman and Boynton found that animals that received cod liver oil stored more vitamin in their lungs than did animals of the same age and diet not receiving cod liver oil, and that the higher intake of this vitamin makes the lung more resistant to disease.

Deficiency in vitamin A, as pointed out by Wolbach and Howe, results in the substitution of stratified keratinizing epithelium for normal epithelium in the respiratory tract, alimentary tract, eyes, para-ocular glands and joints and the urinary tract. Hence, one must assume that with a low intake of vitamin A there will be lowered resistance, so that colds and infections of the respiratory tract will follow.

VITAMINS: THEIR RÔLE IN THE PREVENTION AND TREATMENT OF DISEASE. HENRY F. LANGHORST, M. J. & Rec. **135**:238 (March 2); 265 (March 16) 1932.

In the first article the author points out that vitamin A is fat soluble and stored in the body and that its action is anti-infective and anti-xerophthalmic. Experiments by Mellanby and others to prove its action are given in detail in the article. Foodstuffs that contain this vitamin in abundance are cod liver oil, butter, egg yolk, spinach, turnips, greens, lettuce, carrots, yellow corn and tomatoes. Vitamin B, now called vitamin complex, is found chiefly in yeast, rye, corn, malt, beans, lentils, celery, eggs, milk, vegetables and fruits. Its action is growth promoting; it stimulates the appetite and is concerned in lactation. Pellagra is a deficiency disease dependent on lack of vitamin B. Vitamin B also exerts a favorable influence on calcium and phosphorus utilization.

In the second article, the author discusses vitamin C, the sources from which it is obtained and its action. Vitamin D is then discussed at length. One of the most important actions of this vitamin is that it governs the calcification of bones. Many studies showing the relationship between vitamin D and calcification of bone are given in the article. Vitamin D also plays an important part in the proper growth of the teeth.

WILLIAMSON, New Orleans.

THE CALCIUM-PHOSPHORUS RELATIONSHIP IN THE NUTRITION OF THE GROWING CHICK. R. M. BETHKE, D. C. KENNARD, C. H. KICK and G. ZINZALIAN, Poultry Sc. **8**:257, 1929.

A study was made of the effect of the addition of calcium carbonate and bone meal to the diet of chicks on the formation of bone, as indicated by the ash content of the tibias and the amounts of calcium and inorganic phosphorus in the blood serum. The results indicated that the optimum, or near optimum, ratio of phosphorus for the growing chick lies between 3:1 and 4:1, and that the requirements for the antirachitic factor are at a minimum at this relationship. Within certain limits of concentration, the ratio of calcium to phosphorus is of greater significance in calcification and growth than the amounts of these elements in the ration. The addition of vitamin D, or its equivalent, to the ration or environment of a chick makes possible a greater variation in the calcium-phosphorus ratio and concentration, without seriously interfering with growth and normal formation of bone. Data are given that show that phosphorus may be just as much of a limiting factor as calcium in growth and bone formation of the chick. Limestone high in calcium was more effective than an equivalent amount of calcium in the form of prepared calcium carbonate.

KUGELMASS, New York.

CALCIUM AND PHOSPHORUS METABOLISM OF THE GROWING CHICK. G. DAVIS BUCKNER and J. HOLMES MARTIN, Poultry Sc. **8**:284, 1929.

A study was made of the efficiency of various calcium compounds in promoting the growth of bone in chicks, as indicated by the general development of the chicks and by the amounts of phosphorus and calcium in the ash of the bones of the leg. The results indicated that basic calcium phosphate, alone or with calcium

sulphate or calcium carbonate, caused increased growth and development of the bones of the legs, even though it did not materially influence the percentages of ash in the bones or the percentages of calcium and phosphorus in the ash. Calcium carbonate, calcium sulphate and basic calcium phosphate served equally well as sources of calcium, and the basic calcium phosphate also supplied the required phosphorus. There were indications that a ration made up of yellow corn, wheat middlings and skimmed milk contains enough phosphorus to supplement that in the absorbed egg yolk for the growth of White Leghorn chicks for the first three weeks.

KUGELMASS, New York.

MALNUTRITION DURING EARLY CHILDHOOD. J. LEWIS BLANTON, West Virginia M. J. **28**:163 (April) 1932.

Of the 45,000,000 children in the United States, 6,000,000 are undernourished. It is estimated that 25 per cent of children are undernourished on first entering school. Underweight is only one evidence of malnutrition. Fatigue is one of the most striking evidences in children. Of equal importance is faulty body mechanism, such as "fatigue posture" and "debutante slouch." Among factors of importance that can be controlled at home are: eye strain, diseased tonsils and adenoids, carious teeth, malocclusion and almost all diseases; emotional disturbances at meals and overactivities, school work, music lessons, dancing lessons, movies and the like.

Treatment requires careful study, with parental cooperation, removal of causative factors and supporting measures.

SHAWKEY, Charleston, S. C.

SCORBUTIC HAEMORRHAGE BENEATH THE PERIOSTEUM OF THE FEMUR. H. M. ODDY, Proc. Roy. Soc. Med. **25**:136 (Dec.) 1931.

A patient, aged 10 months, was brought to the hospital on June 17, with the complaint of constant crying since he slipped in the bath several weeks before presentation. On admission the child cried constantly and resented handling. A deep and tender swelling was noted in the region of the left thigh. This was explored, and 20 cc. of fluid containing normal blood cells was withdrawn from beneath the periosteum of the femur. The culture was sterile. Ten days later 12 cc. of fluid was withdrawn; the fluid consisted almost entirely of blood, with some degenerated pus cells. There was some pyrexia for a fortnight. The Wassermann reaction was negative. The report is accompanied by roentgenograms taken before and after exploration.

WILLIAMSON, New Orleans.

TREATMENT OF ACETONEMIC VOMITING OF INFANTS. M. MIRALBELL, But. Soc. catalana de pediat. **1**:25 (July) 1928.

In the acetonemic vomiting of infants there is an uncompensated acidosis with a diminished $p_H$ and alkali reserve and an accumulation of acetone bodies owing to incomplete catabolism of the fats and possibly of the proteins. The treatment consists in administering alkalis and carbohydrates, especially sugar, in order to give sufficient calories, and the injection of insulin. For prophylaxis a diminished intake of fat is suggested, the lower molecular fats being less likely to cause trouble. Calcium caseinate is useful in preventing attacks, but does not aid in the treatment of the attack.

WATSON, Elmhurst, Ill.

THE INITIAL DIARRHEAS IN INFANCY. L. F. MEYER and J. JAHR, Gesundhfürs. f. d. Kindesalt. **7**:1 (Feb.) 1932.

This condition was first described by Davidsohn in 1922. He showed that in practically all young infants who were admitted to the wards of an institution diarrhea developed in the first few weeks of their stay. Finkelstein and Moll have described the same condition. The authors of this article have examined their

records of the last thirty years and have substantiated the results of previous publications. They find that only about 1 per cent of infants below 1 month of age escape an attack of diarrhea in contrast to 66 per cent of the infants between 10 and 12 months; diarrhea develops in 86 per cent of the children in the first two weeks of their stay. It is independent of the type of food and of the season. In the first twenty years of the authors' experience it was seen that diarrhea often led to serious alimentary disturbances, such as intoxication and atrophy, but within the last ten years they have learned to ignore the importance of the initial diarrhea and have stopped giving the child a starvation diet, and so have discovered that practically no serious results follow. In fact, they find that the initial diarrhea is merely an episode. Trouble begins only when the attempt is made to treat such infants with the therapy indicated in serious alimentary disease.

The authors are quite certain that there is no alimentary toxic substance. They doubt the importance of parenteral infections or of an enteral infection of the type of dysentery. They consider that the initial diarrhea is caused by a change in the flora of the intestine, which causes slight disturbances in the peristaltic mechanism of children not in the best of condition. In other words, Meyer believes that the intestinal flora accommodates itself to the flora of the surrounding environment in about the same way as the flora of the respiratory tract does. Therefore, the attempt was made to see whether aseptic nursing could prevent this change.

Each infant was placed in charge of one experienced and reliable nurse. The results were that not a single case of initial diarrhea was seen. The cases that had developed in the ward and in which each patient was placed in charge of a nurse improved immediately. When three children were placed in the charge of one nurse, the first cases of initial diarrhea were seen. These results were obtained even when the children were left in the ward among other infants suffering from initial diarrheas.

The authors believe that an adaptation to the new bacterial flora occurs in these children, but that the improvement in general condition produced by individual nursing prevents any disturbances in the normal mechanism of the body. They believe that the good results were obtained because the nurses were able to adapt the feeding times and amounts of food to the individual needs of each child. They call attention to the work of Pavlov and express the belief that the mental contentment of the infants permits a regular intestinal peristalsis and secretion of the digestive juices. They also call attention to the fact that hospitalized infants are known to sleep less deeply and for shorter periods of time than infants at home. The infants under individual nursing showed the same duration of sleep as those at home.

REICHLE, Cleveland.

SUGAR IN THE TREATMENT OF ACUTE DIARRHEAL DISORDERS OF INFANCY. E. SCHIFF, Jahrb. f. Kinderh. **134**:255 (Feb.) 1932.

For six years, Schiff has begun the treatment of every infant with severe diarrhea by feeding a carbohydrate mixture: one-third Ringer's solution, two-thirds 10 per cent rice water, and from 6 to 8 per cent dextrose. All milk is withheld until the clinical condition improves. In toxicosis, Schiff gives repeated intravenous injections of a mixture containing equal parts of Ringer's solution and 10 per cent dextrose, and from 0.2 to 0.3 cc. of epinephrine, 1:1,000 every two to three hours. His results seem excellent and raise serious doubts regarding the supposed causative rôle of carbohydrate fermentation in diarrhea.

CLAUSEN, Rochester, N. Y.

THE INFLUENCE OF RAW AND AUTOCLAVED MILK ON GROWTH AND METABOLISM. WERNER CATEL, Jahrb. f. Kinderh. **134**:278 (Feb.) 1932.

Autoclaved goat's or cow's milk was given ad libitum to one of twin kids. To the other twin was offered raw milk in a quantity which by calculation was the same on the basis of body weight. The animal receiving raw milk grew much

faster. The increase of body weight in grams per day due to 100 calories of food (*Anschlagswert*) was much higher when raw goat's milk was used. The utilization of fat, protein, carbohydrate and minerals was better. With feeding of autoclaved milk, marked retention of chloride was observed. The addition of dried yeast, of viosterol or of lemon juice tended to improve the diet in all respects.

CLAUSEN, Rochester, N. Y.

THE GAS METABOLISM IN OBESITY IN CHILDHOOD. M. DE BRUIN, Jahrb. f. Kinderh. **134**:330 (Feb.) 1932.

In fifteen obese children, the height was somewhat above the average, but the basal metabolic rate was normal. The specific dynamic action was probably low. A preparation of anterior hypophysis given by mouth did not affect growth or metabolism, but seemed to increase the sense of well-being.

CLAUSEN, Rochester, N. Y.

NITROGEN METABOLISM IN CHILDREN IN CONVALESCENT CAMPS. H. SCHADOW and F. ROELOFFS, Monatschr. f. Kinderh. **52**:50 (Feb.) 1932.

The nitrogen balance was determined in nine children who lived in Hamburg but who were sent to the sea-coast for periods during the winter and summer. Six were studied with particular care. There was unquestionably a better retention of nitrogen during the time spent at the seashore, and this continued for some time after the return to Hamburg.

GERSTLEY, Chicago.

THE FINDING OF ANTIBODIES TO EGG AND MILK IN THE BLOOD SERUM. ALEXANDER STROBL and ALFRED WASITZKY, Monatschr. f. Kinderh. **52**:95 (Feb.) 1932.

Two hundred and forty-four serums of new-born infants, older children and adults were tested for antibodies to the albumin of egg and cow's milk. The serum was positive in 15 of 100 new-born infants, in 13 of 25 nurslings, in 8 of 25 older infants, in 7 of 29 children over 1 year of age and in 5 of 25 adults.

The positive findings could not be related to nutritional disturbances or exudative manifestations.

The antibodies were often found in children nursed exclusively at the breast. In these cases the mother's serum was also positive.

That the sensitization occurs during pregnancy is suggested by the fact that in 100 cases, the blood from the cord gave positive reactions in 15.

GERSTLEY, Chicago.

ACIDITY OF THE SPINAL FLUID IN ALIMENTARY INTOXICATION. HILDE BRUCH, F. VON GRAEVENITZ and S. ROSENBAUM, Monatschr. f. Kinderh. **52**: 135 (Feb.) 1932.

Studies of the hydrogen ion concentration, alkali reserve and total carbon dioxide in alimentary intoxication during the early stages showed no change in the first but a diminution in the last two. With the onset of deep respiration, the total carbon dioxide diminishes somewhat, the alkali reserve decreases considerably more, and the hydrogen ion concentration is increased. There are, however, numerous exceptions to this rule, in which all of these remain normal. In view of these findings the writers conclude that the deep breathing is not necessarily due to a local acidosis affecting the breathing center.

GERSTLEY, Chicago.

THE INFLUENCE OF RICKETS ON THE DEVELOPMENT OF THE JAW AND TEETH. J. KIRSCH and S. ROSENBAUM, Monatschr. f. Kinderh. **52**:177, 1932.

Twenty children were followed during the period of infancy and childhood. Special observations were made as to the relation of any rickets to defects in the

jaw and abnormalities in the teeth. Normal children were compared with groups showing mild rickets and with other groups showing severe rickets. It was concluded that underdevelopment of the jaw occurs exclusively in children who have had rickets. Caries of the milk teeth may occur in perfectly normal children. It is perhaps more common in children with severe rickets. Caries of the second teeth is rare in normal children—occurring in only one in thirteen. It occurred in 50 per cent of the rachitic ones. Delayed teething may occur in the normal child.

GERSTLEY, Chicago.

THE ACID-BASE RELATIONSHIP IN THE YOUNG ORGANISM. A. HOTTINGER and G. HOTTINGER, Monatschr. f. Kinderh. **52**:204, 1932.

The studies now reported by Hottinger and Hottinger confirm their previous observations that there is a definite increase in the excretion of organic acids in the urine during florid rickets. This sinks to normal during recovery. Ammonia and amino-acids follow the same rules. This increase does not occur in the early stages and so cannot be used for an early diagnosis. If tetany complicates florid rickets, the results of the urinalyses become normal. The excretion in a woman seven months pregnant was normal. The excretion is increased in atrophy, associated either with diarrhea or with starvation, as in pyloric stenosis. It is particularly increased in diabetes. Of exogenous factors having influence, treatment with a quartz lamp increases the excretion; withdrawal of water has no effect; in perspiration, acids are excreted through the skin; changing from cow's milk to breast milk diminishes excretion; addition of protein has no effect as long as excretion of nitrogen is not increased; addition of fat normally has no effect, but in rickets causes an increased excretion; a diet high in carbohydrate and low in fat and protein diminishes the excretion.

GERSTLEY, Chicago.

LOSS OF APPETITE IN CHILDREN. JADWIGA FRÜHAUFOWA, Pediat. polska **11**: 188 (May-June) 1931.

The author discusses the causes of loss of appetite, enumerating them as eating between meals, lack of exercise and being spoiled. He gives Siegfried's and Wolff's method of treatment. The child is starved for from four to six days; that is, on the first day he receives tea five or six times; the second day, two tablespoonfuls of milk and two of water five or six times; the third day four tablespoonfuls of milk and four of water five or six times, and the fourth day six tablespoonfuls of milk and six of water five or six times. After starvation, the child is given 8 ounces of milk at 7 a. m.; at 8 a. m., a bun, butter and honey; at 9 a. m., egg yolk, lemon and sugar; at 10 a. m., bacon; at 11 a. m., fruit; at 12:30, a dish of a vegetable, two pieces of meat and gravy and legumin. He then sleeps for two hours. At the fifteenth hour, 8 ounces of milk are again given; at the sixteenth hour, a bun, butter and cheese; at the seventeenth hour, an egg; at the eighteenth hour, fruit and at the nineteenth hour, a vegetable and meat. After each meal the child feels hungry.

KRUPINSKI, Chicago.

THE VITAMIN C IN GOAT AND COW MILK. J. C. DE RUIJTER DE WILDT and E. BROUWER, Versl. landb. Onderzoek Rykslandbouwproefsta **36**:15, 1930.

Guinea-pigs were used to test the content of vitamin D in goat and cow milk. Milk obtained during the summer, when the animals were at pasture, and during the winter, when they were stall fed, was tested. No significant difference between the content of vitamin C in goat and cow milk was evident during the course of the experiment. No seasonal variation in the content of vitamin C was observed.

KUGELMASS, New York.

## Acute Infections

ADVANTAGES OF TOXOID IN DIPHTHERIA PROPHYLAXIS. WALTER T. HARRISON, Am. J. Pub. Health **22**:17 (Jan.) 1932.

In discussing the advantages of toxoid over toxin-antitoxin in immunization against diphtheria, the author states that the original 5 L + doses of toxin-antitoxin frequently caused a severe reaction. When the amount was lowered, in 1922, to a 0.1 L+ mixture, practically no reactions occurred. The immunizing property, however, remained the same. This is compared with the fact that toxoid occasionally gives cutaneous reactions in children over 7 years of age.

The disadvantages of toxin-antitoxin are: 1. It is thought to sensitize to the serum used in its preparation. 2. Freezing and age may increase the toxicity or lower the immunizing properties and may account for the variation in results in different series. 3. Three injections are required.

Diphtheria toxoid came into use through Ramon in 1923. It is made by adding a dilute solution of formaldehyde, U. S. P., to toxin and subjecting the mixture to a temperature of from 39 to 40 C. until toxicity is lost, which usually takes from three to six weeks. There is no serum present in toxoid. Two injections of 1 cc. are given at intervals of from three weeks to one month. Few reactions occur in persons under the age of 7 years. In persons over this age cutaneous irritations occur more frequently, and a skin test should be made.

The advantages of toxoid are: (1) It is from 20 to 30 per cent more effective than toxin-antitoxin, (2) it contains no serum, (3) it contains no free toxin and (4) it is more stable to temperature and age.

PARKER, Rochester, N. Y.

EXPERIENCES WITH DIPHTHERIA TOXOID IN CANADA. FITZGERALD, DEFRIES, FRASER, MALONEY and MCKINNON, Am. J. Pub. Health **22**:25 (Jan.) 1932.

Toxoid has been used in Canada since 1925, during which time more than 1,000,000 persons have been treated. The toxoid was made and tested according to the method of Ramon. Two periods of treatment were used. Of the persons receiving two doses of 0.5 cc. each, 70 per cent were immunized, and there was a reduction in mortality from diphtheria of 74 per cent. Of those receiving three doses of 0.5, 0.5 and 1 cc., 90 per cent were immunized, and the reduction in mortality was 90 per cent. In several large communities diphtheria was practically eliminated.

PARKER, Rochester, N. Y.

DEGREE OF IMMUNIZATION FROM INJECTION OF DIPHTHERIA TOXOID. O. R. POVITZKY, Am. J. Pub. Health **22**:29 (Jan.) 1932.

The author notes that standards for measuring the antigenic property of toxoid are still not quite satisfactory. The National Institute of Health requires a minimum of 5 L+ doses per cubic centimeter in the original toxin used for the preparation. Ramon requires 10 antigenic units per cubic centimeter of toxoid. This is measured by Ramon's flocculation test. By this method the author tested various products and found variations from no antigenic units to a maximum of 7 antigenic units per cubic centimeter. This method makes possible titrations of toxoids to determine their value.

After trying various intervals between injections, the author concluded that the optimum interval is three weeks after the first and two weeks after the second, three doses being the most effective.

The use of alum in the preparation enhances the value of the final product.

PARKER, Rochester, N. Y.

THE PREPARATION OF STABILIZED SCHICK TOXIN. P. J. MOLONEY and EDITH M. TAYOR, Am. J. Pub. Health **22**:38 (Jan.) 1932.

Schick toxin diluted with saline solution alone is very unstable. The authors found that toxin diluted with a borated saline solution containing gelatin is rela-

tively stable. They conclude that a 1:4 dilution of Sorensen's buffer solution of $p_H$ 8, containing sodium chloride 0.85 per cent and gelatin 0.02 per cent, is a suitable diluent for the preparation of Schick toxin. PARKER, Rochester, N. Y.

STUDIES IN BLACK-WATER FEVER. U. BRAMACHARI, P. BRAMACHARI and R. BANERJEA, Am. J. Trop. Med. **12**:117 (March) 1932.

The authors carried out experiments in vitro to determine, if possible, whether there was any difference in the behavior of the erythrocytes to solutions of quinine in persons in whom black-water fever developed and in those in whom it did not develop. Also, to determine whether there was any difference in vulnerability in the erythrocytes to quinine in persons in whom black-water fever developed before, during and after hemoglobinuria.

They found the erythrocytes in cases of black-water fever following the administration of quinine slightly more vulnerable to quinine than in normal persons, but not sufficiently to account for the black-water fever. In patients in whom black-water fever developed they found no difference in the behavior of the erythrocytes to quinine before, during or after hemoglobinuria.

BURPEE, Augusta, Ga.

TOXIC ENCEPHALOPATHY IN MEASLES. ARMANDO FERRARO and I. H. SCHEFFER, Arch. Neurol. & Psychiat. **27**:1209 (May) 1932.

The authors point out that the pathologic changes in encephalitis following measles resemble those seen in vaccine encephalitis, influenzal encephalitis and rabies vaccine encephalitis. The typical lesions are: first, perivascular proliferation; second, perivascular demyelinization, and, third, pronounced involvement of the white substance. The two cases reported did not show the first and second symptoms, and there was involvement of the gray substance. There was, however, absence of inflammatory lesions. The findings in these two cases are due to the severity of the process, and unquestionably are toxic in origin.

BEVERLY, Chicago.

FURTHER STUDIES UPON THE EFFECT OF VARIOUS CARBOHYDRATES ON PRODUCTION OF DIPHTHERIA TOXIN WITH SPECIAL REFERENCE TO ITS FLOCCULATING TITER AND FINAL $p_H$. ELIZABETH LEE HAZEN and GEORGE HELLER, J. Bact. **23**:195 (March) 1932.

As early as 1896 Park and Williams recommended the use of dextrose in small quantities as an aid in the production of toxic filtrates from Corynebacterium diphtheriae. The authors in the present study found that carbohydrates are essential for the production of toxic filtrates of C. diphtheriae possessing highest potency. Dextrose in small amounts is definitely superior to maltose, dextrin or glycerin as an aid to production of toxin. Larger amounts of maltose than it is possible to use in dextrose without adjustment of the hydrogen ion concentration increase the *Lf* titer of the filtrates of C. diphtheriae. Filtrates of the highest *Lf* were obtained with a combination of dextrose in a concentration of 0.15 per cent and maltose in a concentration of 0.3 per cent. The term *Lf* is used by the author in accordance with Glenny and Wallace's definition indicating "that amount of toxin (corresponding to one unit of a certain antitoxin) in that mixture which flocculates most rapidly when a series of mixtures of that toxin and antitoxin are set up in varying proportions and observed under constant conditions."

STOESSER, Minneapolis.

MILK-BORNE SEPTIC SORE THROAT AND SCARLET FEVER AND THEIR RELATION TO BETA HEMOLYTIC STREPTOCOCCI. ANNA W. WILLIAMS and CAROLINA R. GURLEY, J. Bact. **23**:241 (March) 1932.

The authors present a short review of the present status of Streptococcus epidemicus as a species and also try to show that neither of the characteristics

claimed as the only species characteristics — capsule formation and moist growth on blood mediums — holds sufficiently to be used in designating a species, and that at present strains of hemolytic streptococcus from septic sore throat not otherwise placed by agglutinin absorption should be termed simply S. hemolyticus. Since 1900, milk-borne epidemics of septic sore throat have been considered by the majority of physicians as comprising a clinical entity. It is on this opinion of clinical entity that Davis laid the chief stress in his review of this subject at the meeting of the American Medical Association in 1929, when he reiterated his claim that the streptococcus isolated by him in 1912 from a milk-borne epidemic of sore throat and called by him S. epidemicus is a distinct species and the cause of this disease. From time to time, outbreaks have been reported as giving a varying clinical picture; and scarlet fever as well as erysipelas and other septic conditions have been observed in the same epidemic. On the other hand, the authors conclude from their studies on this subject that milk-borne epidemics of septic sore throat and of scarlet fever may be caused, respectively, by one or several agglutinative types of hemolytic streptococci. When scarlet fever predominates, the epidemic strain usually belongs to one of the common scarlet fever agglutinative types; when septic sore throat predominates, the epidemic strain may be one of several agglutinative types, two of which have been demonstrated in these studies and have been tentatively named S. epidemicus, agglutinative type I and S. epidemicus, agglutinative type II.

STOESSER, Minneapolis.

SOME CLINICAL OBSERVATIONS ON THE MEASLES EPIDEMIC OF 1931 IN ST. LOUIS. JOHN ZAHORSKY, J. Missouri M. A. **29**:5 (May) 1932.

The author feels that the only factor in the epidemiology of measles is the presence of a large number of non-immune persons in the community. He prefers to treat measles in the home.

A résumé is given of 300 cases occurring in 1931 in which the patients were treated by the author and by Dr. T. S. Zahorsky without fatality.

The routine treatment consisted of rest in bed for one week, fluids and alkalis. Salicylates were sometimes employed, but no attempt was made to allay the fever. Antipyretics were not favored on the theory that they might interfere with the proper resistance of the body.

In one case convalescent serum was used; immune serum was used as a prophylactic only in very young children. This was usually obtained from the mother. Following the theory of Knaur that the person who has been in the sick room and inhaled the poison of measles repeatedly has a higher concentration of antibodies toward the disease, mothers who had nursed a patient with measles were preferred.

The author found the complications about as numerous as those reported in other epidemics.

Two cases of encephalomyelitis were reported; in both the patients recovered.

BERGER, Kansas City, Mo.

ARGUMENTS IN FAVOR OF COMPULSORY VACCINATION FOR PRIVATE SCHOOL CHILDREN. SAMUEL B. WOODWARD, New England J. Med. **206**:570 (March 17) 1932.

The author's arguments contained in a report presented before the Public Health Committee of the Massachusetts Legislature, on Feb. 25, 1932, are convincing. Referring to a circular (with a map of the United States) sent out by the citizens' committee opposing compulsory vaccination, he says: "Nine states are in black. These states have some form of compulsory vaccination. "Six states appear in stripes. Here vaccination is optional with local authorities.

"Thirty-three states are in white. In these no compulsory vaccination laws exist.

"Four gold-starred states have, according to the circular, passed all the rest in the race for freedom for they prohibit compulsory vaccination. These four

states, Arizona, Utah, North Dakota and Minnesota, with a combined population in 1920 of 3,817,555 persons accumulated in their race for freedom in the ten years 1919-1928, 46,130 cases of smallpox, while Massachusetts with a population slightly larger than their combined total, i. e., 3,852,356, had but 408. The free states had in other words 113 times as much smallpox as did we, and Utah taken by itself 272 times as much. Furthermore, the four states in question, Utah, Arizona, North Dakota and Minnesota, had more than twice as many cases of smallpox as all the black states combined with their 29,472,362 inhabitants, for these same black states had during the years in question but 20,571 cases, 13,496 of which were in the two states of South Carolina and Kentucky. Fifteen times as much smallpox man for man seems to me a rather high price to pay for this boasted freedom.

"The local option states, North Carolina, Georgia, Oregon, New Jersey, Ohio and Connecticut with a population of 16,534,260 had 91,985 cases, while the no compulsory law states with their 57,636,032 inhabitants harbored the remaining 401,045 cases of smallpox. How, under these circumstances, does the Citizens' Committee dare to say that wherever compulsory vaccination has been abandoned and sanitation installed in its place, smallpox has been wiped out?"

"Utah with less than half a million inhabitants had during the 10 years previously spoken of over 4,000 more cases of smallpox than all New England with New York, Pennsylvania, New Jersey and Maryland thrown in for good measure, with a combined population of 31,111,714, or about 13,000 cases for the 434,000 people in Utah, and 8,000 for the 31,000,000 of the states just mentioned."

"There is absolutely no argument for compulsory vaccination of children in public schools and a refusal to provide the same protection for those attending private and parochial schools. In parenthesis may I say that the City of New York, which vaccinates all pupils, teachers, janitors, etc., in all schools, had in the ten years 1921-1930 but 104 cases of smallpox and no deaths and, lest it be again said that only public school children are to be vaccinated under the law, the State Supreme Court has ruled that the word school in the status means any school, public or private."

GENGENBACH, Denver.

CURRENT PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES. Pub. Health Rep. **47**:1147 (May 20) 1932.

For the period from March 27 to April 23, 1932, the cases of influenza, typhoid fever and scarlet fever showed a slight increase over the corresponding period in 1931. Cases of diphtheria, measles, smallpox and meningitis were fewer. The average mortality was 13.5 per thousand of population.

SANFORD, Chicago.

PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES. Pub. Health Rep. **47**:1285 (June 10) 1932.

For the period from April 24 to May 21, 1932, the incidence of diphtheria, smallpox and influenza was lower than is usual in the corresponding periods. The incidence of scarlet fever and of measles was normal. There was a rise in meningococcus meningitis. Poliomyelitis was at the seasonal low level, twenty cases being reported; ten occurred in California, six in Illinois and four each in New York, New Jersey, Ohio and Wisconsin. The average mortality was 11.6 per thousand.

SANFORD, Chicago.

THE RELATIVE VALUE OF SOME DIPHTHERIA PROPHYLACTICS AND THE PRINCIPLES OF ACTIVE IMMUNIZATION VERSUS DIPHTHERIA. SHELDON F. DUDLEY, Quart. J. Med. **1**:213 (April) 1932.

This paper is offered as an appendix to the author's paper, entitled "Critical Review of the Schick Test and Its Applications" which appeared in the *Quarterly Journal of Medicine* (**22**:321, 1928-1929).

Dudley reports the results of various diphtheria prophylactics as tested on the personnel of the Greenwich Hospital School. The work is discussed under the following headings: (1) Introduction; (2) Toxoid versus "Floccules"; (3) The Refractory Schick Susceptible; (4) English versus French Toxoid, (5) Toxoid versus Toxin-Antitoxin, (6) Reactions After Toxoid and "Floccules"; (7) Mass Immunization of the General Population; (8) Some Principles of Practical Active Immunization Against Diphtheria, and (9) Conclusion.

The author found that full strength English toxoid and the most concentrated (strong) "floccules" were both most satisfactory antigens. At three months, both antigens had immunized 97 per cent of the boys to whom they were given. The immunizing powers of the French and English toxoid were found to be equal. Toxoid was found to be a much more powerful antigen than the toxin-antitoxin mixture. The author states: "All things considered, toxoid should take the place of toxin-antitoxin for routine active immunization against diphtheria, and the latter antigen be permanently relegated to an honorable place in the history of preventive medicine." He believes that if 80 or 90 per cent of children under 10 years of age could be maintained in a condition to give a negative reaction to the Schick test diphtheria would, for practical purposes, vanish within five years.

BRADFORD, Rochester, N. Y.

THE ELECTROCARDIOGRAM IN DIPHTHERIA. STANLEY ALSTEAD, Quart. J. Med. **1**:277 (April) 1932.

The object of this investigation was to study the changes usually seen in the electrocardiogram during diphtheria, to correlate them with the clinical condition and to assess the value of the results in a fever hospital.

One hundred cases were taken, including mild (23 per cent), moderate (32 per cent) and severe (45 per cent) cases.

The clinical abnormalities that were considered to indicate diphtheritic myocarditis were: (1) persistent tachycardia or bradycardia; (2) heaving cardiac thrust; (3) migration of the apex beat farther from the midline; (4) changes in the character of the first sound, especially softening of the first sound in the mitral area, splitting of the first sound and excessive booming of the heart sounds; (5) alteration in the heart rhythm to a "triple" or "gallop" type; (6) deterioration of the general condition of the patient, such as pallor, restlessness or apathy, vomiting, enlargement of the liver with abdominal tenderness, rapid, easily compressible pulse and fall in blood pressure, and (7) abnormal responses to increasing physical effort as indicated in the pulse rate, extrasystoles or sinus arrhythmia appearing during the course of the disease.

In the electrocardiogram the abnormalities commonly found are: (1) conductive lesions, intraventricular block, bundle branch and complete auriculoventricular dissociation and (2) lesions myocardial in origin without gross involvement of the specialized conducting system.

The author concludes that, of the various physical signs indicative of myocarditis in diphtheria, the most valuable as confirmed by simultaneous electrocardiographic records are: (1) progressive softening of the first heart sound; (2) migration of the apical impulse, and (3) occurrence of a triple rhythm.

Except in the event of complete heart block, no retrace can be placed on the electrocardiographic findings in diphtheria in judging the prognosis.

BRADFORD, Rochester, N. Y.

DIPHTHERIA. P. UHRY, Nourrisson **20**:94 (March) 1932.

This article reviews a recent monograph on diphtheria by Debré and Ramon. Some points particularly emphasized are as follows: 1. There is no relation between the size and morphology of Bacillus diphtheriae and its virulence. 2. Virulence and toxigenicity are independent of each other. 3. Persons retaining one-thirtieth unit of antitoxin per cubic centimeter of blood serum, as shown by a negative Schick test, are usually immune. 4. The disease is spread more by carriers than by contacts.

MCCLELLAND, Cleveland.

QUARANTINE FOR SCARLET FEVER. A. B. MARFAN, Nourrisson **20**:97 (March) 1932.

In France, scarlet fever patients are isolated for forty days. Marfan believes that this is too long for mild cases and too short for severe cases or those with complications. He argues for a minimum isolation period of twenty-five days. His criteria for lifting the quarantine are: a five-day afebrile period, a throat that appears normal and the absence of cervical adenopathy or other complication. He places most reliance on the appearance of the throat.

McCLELLAND, Cleveland.

ANTIDIPHTHERITIC VACCINATION WITH ANATOXIN. G. RAMON and R. DEBRÉ, Presse méd. **40**:601 (April 20), 1932.

The percentage of successful vaccinations against diphtheria with anatoxin may be greatly increased by using anatoxin of a higher titer than the ordinary commercial anatoxin, which has a titer of approximately 10 anatoxic units per cubic centimeter. By using anatoxin with a titer of 16 units, with three injections of 1 cc., 1 cc. and 2 cc. at intervals of three weeks, negative Schick reactions were obtained in 123 children who previously showed positive Schick reactions. While two injections confer immunity in most cases, a third injection increases the percentage of negative reactions. Experiments with "associated vaccination" using anatoxin in combination with antityphoid vaccine have shown very good results, the anatoxic titer of the patient's serum being not merely the one-tenth unit necessary for immunity, but in 60 per cent of the cases, higher than 1 unit, and in some cases even as high as 30 or 40 units.

Vaccination by the nasal route is sometimes practiced in very delicate subjects, or those sensitized by previous injections, but this method is neither practical, economical nor sure.

In time of epidemics, when exposure is known to have occurred, anatoxin may be given along with prophylactic doses of serum (injecting the anatoxin first). The danger of the so-called "negative phase" is overestimated and may be disregarded.

BIEKER, St. Petersburg, Fla.

THE EFFICACY OF ANTIDIPHTHERITIC SEROTHERAPY. S. DE STAFANO, Pediatria **40**:479 (May 1) 1932.

The author presents a report of his own observations and those of others, critically noting the mortality rate from diphtheria both in epidemic and in non-epidemic periods. He demonstrates that in spite of the reduction observed in late years the mortality from this disease is higher than is apparently justifiable. Attempting to determine the causes responsible for this high rate, he concludes that they may be assigned as follows: (1) diagnosis being made late in the course of the disease; (2) the omission of administration of serum; (3) the use of an insufficient amount of serum; (4) the use of serum that is too old, and (5) to a certain extent the virulence of a particular epidemic, and whether the disease is associated with other complicating pathologic organisms.

SIGNORELLI, New Orleans.

A CASE OF MEASLES IN A NEW-BORN INFANT, FIFTEEN DAYS OF AGE. L. IASILLI, Pediatria **40**:489 (May 1) 1932.

A case of measles in a child 15 days of age is reported, with a detailed description of the clinical manifestations. The case developed during an epidemic.

SIGNORELLI, New Orleans.

PROTECTIVE SERUM AND IMMUNITY IN MEASLES. R. DEBRÉ, Arch. f. Kinderh. **95**:169, 1932.

The author reports four groups of cases showing that a child exposed to measles and receiving convalescent serum does not gain lasting immunity to this

disease unless the modified measles presents the definite clinical symptoms of true measles in the form of fever lasting several days, coryza, cough and cutaneous manifestations.

LESLIE, Evanston, Ill.

THROMBOPENIC PURPURA FOLLOWIMG SMALLPOX VACCINATION. A. DORMANN, Monatschr. f. Kinderh. **53**:204, 1932.

A 7 months old child was vaccinated against smallpox, and seven days later purpura, with bleeding into the skin and intestine developed. The bleeding time was normal, and the Rumpel-Leede phenomenon remained negative for three minutes. Thrombocytes were reduced to 68,000. Against the diagnosis of thrombopenic purpura was the normal bleeding time, but the writer says that this variation occurs in children.

Three other cases of this type following vaccination have been reported.

GERSTLEY, Chicago.

GASTRIC HEMORRHAGE IN TYPHOID FEVER. P. G. EIWIN, Monatschr. f. Kinderh. **53**:220, 1932.

A 10 year old boy, following several days of fever at home, was suddenly seized with vomiting of blood and intestinal hemorrhages. A positive Widal test showed the condition to be typhoid fever.

GERSTLEY, Chicago.

THE TOXIN-ANTITOXIN CONTENT OF THE SPINAL FLUID IN POSTDIPHTHERITIC PARALYSIS. ROBERT QUEST, Monatschr. f. Kinderh. **53**:225, 1932.

In nine cases of postdiphtheritic paralysis, lumbar punctures were performed and the fluid tested for its content of toxin and antitoxin by means of guinea-pig inoculation. In none of these could any diphtheria toxin or antitoxin be demonstrated.

GERSTLEY, Chicago.

THE IRRITABILITY OF PERIPHERAL NERVES IN POSTDIPHTHERITIC PARALYSIS. ROBERT QUEST, Monatschr. f. Kinderh. **53**:229, 1932.

The writer determined the electrical irritability of the peripheral nerves in postdiphtheritic paralysis. He found that this frequently increased, even reaching the measurements found in spasmophilia. Chemical examination of the blood in three of these children showed a diminution in serum calcium. Possibly the diphtheria toxin affected the parathyroid.

GERSTLEY, Chicago.

FOLLOW-UP EXAMINATION IN TWENTY-SEVEN CASES OF POSTVACCINAL ENCEPHALITIS. O. KUDELKA, München. med. Wchnschr. **79**:379 (March 4) 1932.

Kudelka examined sixteen girls and eleven boys in whom encephalitis developed from 1928 to June, 1931, following vaccination against smallpox. At the time of vaccination the children were all over 4 years of age. Judging from the appearance of the scars, the original local reactions had been severe. Some children had hyperactive reflexes and one, in whom encephalitis developed in May, 1931, had unilateral paralysis of the abducens nerve. In view of the complete recovery of other children who had severe symptoms (speech paralysis), the prognosis was considered favorable. In contrast to other forms of encephalitis, there were no mental or behavior disturbances. Some of the children were considered by their teachers the best pupils in the class. From his observations Kudelka concludes that postvaccinal encephalitis results either in death or in complete recovery.

BRAHDY, Mount Vernon, N. Y.

SCARLET FEVER AT AN EARLY AGE. A. A. TOMILILIN, Pediatriya **14**:416, 1930.

The symptoms of scarlet fever at an early age are dealt with briefly in medical literature. Some authors point out that scarlet fever does not exist until the age of 6 months. On the other hand, cases of scarlet fever among children still being fed at the breast have been reported. According to Dr. Yoffe, 4 per cent of the children in the Charcov Hospital under 1 year of age were afflicted with scarlet fever.

The purpose of the work summed up in this article is not only to determine the frequency of infection and the percentage of fatal cases but also to follow the clinical course of scarlet fever, its symptoms and development, and to study the character and frequency of complications as a result of scarlet fever.

The study was conducted during the period from 1922 to 1927. Seven hundred and forty-one patients were treated; of these thirty-three, or 4.4 per cent, were under 1 year of age and ninety-seven, or 13 per cent, were under 2 years.

According to this study, 48 per cent of the patients were boys, and 52 per cent, girls. According to Dr. Aksenor and Dr. Yoffe, boys are infected more frequently.

The seriousness of scarlet fever is divided into three categories: light, medium and grave. The study definitely indicated that the majority of infections due to scarlet fever among children up to 2 years of age are of the light and medium form.

The beginning of scarlet fever is sudden and sharp, usually in the midst of good health and accompanied by a rise in temperature. The highest temperature observed at the beginning of scarlet fever was 40 (Réaumur). Vomiting was observed at the beginning of the illness in thirty-four cases, that is, in 38.6 per cent. In eighteen cases, 20.4 per cent, it was repeated.

The eruption appeared usually on the first day; the latest observed was on the fifth day. The eruption disappeared within from five to ten days and was followed by a scaly desquamation.

The second stage of scarlet fever is characterized by cardio-arterial disturbance. The scarlatina heart was established in 72 per cent of the cases as consisting of enlargement of the heart, arrhythmia and slow pulse. The scarlet fever heart appears on from the third to the tenth day of the disease and continues for from two to six weeks. Occasionally a child was discharged with cardiac symptoms persisting. Change of blood pressure was observed in patients with scarlet fever; in twenty-four it was of the light form, in forty of the medium, and in five of the grave form. With the appearance of the scarlet fever heart the blood pressure falls. It may be generalized that the blood pressure rises in the first period of the disease and falls during the second. In the group afflicted with the light form of scarlet fever the blood pressure remained normal in three patients but gradually increased in others.

The most frequent complication of scarlet fever is otitis media. Of a total of forty-eight patients 54.5 per cent were treated for otitis media. In 33 per cent of the patients the condition was purulent otitis media, and nineteen patients, or 21.5 per cent, suffered from catarrhal otitis media. The secondary complications, in order of frequency, are lymphadenitis and nephritis.

Tomililin concludes that scarlet fever rarely occurs before 6 months of age; it occurs before 1 year in only 4.4 per cent, and between 1 and 2 years in 13 per cent. He says that sex has no bearing on the probability of infections; in frequency of infection, the medium and light forms of scarlet fever occupy the first and second places. The grave form occurs rarely; the clinical symptom complex at an early age differs little from that at a later age. Scarlet fever heart appears to be the constant symptom of scarlet fever at an early age. Complications as a result of scarlet fever in the order of frequency of occurrence are otitis media, purulent or catarrhal, lymphadenitis, nonabscessed and abscessed, and, rarely, involvement of the kidneys. The death rate from scarlet fever in patients up to 1 year of age in forty-two cases was 45 per cent. YAMPOLSKY, Atlanta, Ga.

## Chronic Infections

UNDULANT FEVER IN CHILDHOOD. HENRY DIETRICH and CHARLES W. BONYNGE, J. Pediat. **1**:46 (July) 1932.

The history and literature on undulant fever are briefly reviewed. The bovine, porcine and melitensis (or caprine) strains of Brucella abortus are now recognized. The melitensis strain shows the greatest pathogenicity for man. Contact with infected animals is a more important factor in transmission to man than drinking infected raw milk. It is noteworthy that the incidence of undulant fever in children is much lower than in adults, for which the authors propose the following explanations: lack of contact with infected animals, low pathogenicity of the bovine variety, especially when ingested, small number of organisms ingested and biologic immunity of the tissues of the small child. Routine agglutination and complement-fixation tests on several large groups of children yielded results varying from none to 17 per cent positive reactions.

LEMASTER, Evanston, Ill.

STOVARSOL IN THE PERORAL TREATMENT OF CONGENITAL SYPHILIS. ARTHUR F. ABT and ALFRED S. TRAISMAN, J. Pediat. **1**:172 (Aug.) 1932.

Twenty-two children with congenital syphilis were treated with stovarsol given by mouth. The literature concerning the use of stovarsol is briefly reviewed. Stovarsol was used in daily doses of 5 mg. per kilogram of body weight, gradually increased to 20 mg., during a nine weeks' course, followed by six weeks of rest. Mild diarrhea occurred in two patients, and arsenical dermatitis in two others, one case ending fatally. The syphilitic lesions healed rapidly. Gain in weight and rise in hemoglobin were marked during treatment. The Wassermann reaction was negative in 59 per cent of the children after one course of treatment.

The authors conclude that stovarsol given by mouth is the treatment of choice in congenital syphilis.

LEMASTER, Evanston, Ill.

THE PROBLEM OF THE CHILD IN THE TUBERCULOUS HOUSEHOLD. R. C. WINGFIELD, Brit. M. J. **2**:787 (Oct. 31) 1931.

The author discusses in an intelligent, dispassionate and carefully analytical manner the general problem of the tuberculous child. He points out first that in any community, regardless of varying statistics, the contact child is more frequently affected than those who are not in contact with the disease. The second point is in answer to the question: "Does the contact child run greater risks of immediate sickness or death from tuberculosis than the average child?" Statistics are quoted as well as the opinions of authoritative investigators and the answer is again strongly affirmative. The third point is discussed as an answer to the question: "Is the contact child exposed to greater risk of future sickness or death from tuberculosis than the average child?" In answering this question the author admits the depth of the water to be navigated. It is quite likely, in his opinion, that contact children are not subject to any greater risks from tuberculosis as adults than are noncontact children, but he draws a sharp distinction between contact children and infected children, and here again the differences of opinion by recognized authorities are cited. The author feels that children who have had the childhood type of infection have a certain amount of future protection so far as open, frank adult tuberculosis is concerned. Naturally, as would be expected, he draws a line between the early infection and the later or preadolescent infection. The fourth point discussed is likewise in answer to a question, as follows: "Does the contact child constitute an immediate danger to the community?" The author concludes that he is not an immediate danger to the community. A number of constructive suggestions are then offered. The duty of the public health officer in practicing preventive medicine generally is largely to the population as a whole, whereas the practitioner's duty is mainly a clinical one and to the individual patient. It is necessary to watch all children in tuberculous homes by means of

the intradermal test and other clinical phenomena. It is not so much a single exposure as continued exposure that counts. The parents, or others infected, must be taught how to protect children from themselves. He points out that it is at adolescence that special care must be taken with the contact child. Roentgen examination is particularly useful at this time. This opinion is cited from McPhedran. It is at adolescence that the spinal lesion is known. The author admonishes public health officials to develop a clinical point of view. Hence cooperation between the family physician and the public health official is absolutely essential. Quoting from an American authority the author stresses the fact that thorough, aggressive and prolonged follow-up work after preventorium treatment is more important than the treatment in the preventorium itself. It is seriously debatable whether a child who has come from a tuberculous environment and goes into a preventorium should ever return to that home. Of course, the problem is immediately complicated.

Finally, the question of immunization with B C G is discussed. The author appears to be in about the same state of doubt as are most American writers and observers.

ROYSTER, University, Va.

HUMAN TUBERCULOSIS OF BOVINE ORIGIN. A. STANLEY GRIFFITH, Edinburgh M. J. **39**:177 (March) 1932.

Griffith reviews the investigations regarding the rôle played by the bovine type of tuberculosis in human beings, and then discusses the measures for public health protection. Following Koch's announcement in London, thirty years ago, that infection with bovine bacillus is rare in human beings, the studies that were made in Great Britain, Europe and America show how greatly and tragically Koch was mistaken in this point of view. In Great Britain, especially Scotland, the disease has been found to have a higher frequency than it has in continental Europe and America.

Griffith, of the Medical Research Council, Field Laboratories, the University of Cambridge, gives the results of investigations in England, separately from those for Scotland. The differentiation has been made in about three thousand cases. The manifestations of the disease itself do not enable one to diagnose the type of tubercle bacillus. Lesions and symptoms are the same in both types. In the tables given by Griffith, children under 5 years show the bovine type in the high percentage of 85.7 in disease of the cervical glands, and in that of 57.3 in tuberculosis of the skin. In other sites, the bovine type of the disease occurs in from 34.8 to 29.7 per cent of patients. At least three months are required before an expert can determine the type of bacillus.

The author reports that the bovine type can produce ulcerative pulmonary tuberculosis. Bovine tubercle bacilli will appear in sputum more frequently if this type of bacillus has the opportunity to enter the body, as in the milk for children, in whom there is a high frequency of bovine infection. He feels that in most cases in children the disease of the lung is secondary to infection through ingestion. The milk supply in England and Scotland needs improvement to protect aganist the infection spread from tuberculous cows. Pasteurization and boiling must be urged on communities and enforced by health authorities. The eradication of tuberculosis in cattle is feasible and necessary. The author gives his ideas on the disposition of animals with a positive reaction to tuberculin.

NEFF, Kansas City, Mo.

THE INCIDENCE OF THE HUMAN AND BOVINE TYPES OF TUBERCULOUS INFECTION IN CHILDREN LIVING IN THE WEST OF SCOTLAND. J. W. S. BLACKLOCK, Edinburgh M. J. **39**:190 (March) 1932.

The author, who works in the department of pathology, Hospital for Sick Children, Glasgow, pays tribute to the early workers of the Edinburgh school, who found that Scotland had a high incidence of bovine infection in man. Blacklock mentions the incidence of both types of tuberculous infection among children

in Glasgow and the western part of Scotland. For seven years before 1931, search was made at the hospital in surgical and autopsy material taken from children aged 7 weeks to 13 years. The autopsy material was divided into two classes, in one of which the tuberculosis was connected with the cause of death and in the other the condition was found only accidentally post mortem. Pathologic search was made for evidence as to the primary lesions.

The tabulated figures for autopsy cases show that 27.3 per cent of the cases of tuberculous disease causing death were of the bovine type and 72.7 per cent of the human type. When age is considered, the highest incidence of bovine infection was found in the group of children from 1 to 2 years of age. Primary lesions occurred in the abdomen in more than half of the children under 2 years of age; the figures for Glasgow showed that while the incidence of the human type of the disease was higher at this time of life than at any other age, there was also a large number of cases of bovine infection. Cow's milk for infants under 6 months of age is boiled; the risk of bovine infection is therefore less at that period than it is for the next eighteen months, when milk is not so apt to be boiled.

In the group of cases in which death was not due to tuberculosis, only three cases of primary thoracic infection were found in thirteen hundred consecutive autopsies. In abdominal cases, 86.7 per cent of the lesions were due to bovine infection. The observations suggest that the bovine type may be less pathogenic than the human type.

The incidence of bovine infection is found to be higher in Scotland than in other parts of the world. This is shown in tabulated form. Cervical glandular tuberculosis is more commonly of the bovine type, but in disease of the bones and joints less than 50 per cent of the cases are of the bovine type.

In city children the disease was found more commonly to be in the respiratory tract, caused by the human type of organism. Bovine infections were found more commonly in country children with tuberculosis of the alimentary tract.

NEFF, Kansas City, Mo.

TUBERCULOMA IN CHILDREN. L. BABONNIX, Gaz. d. hôp. **105**:709 (May 11) 1932.

The author groups various case reports according to the main clinical features, i. e., convulsive, hemiplegic, meningitic, cerebellar, neoplastic and silent.

KAJDI, Baltimore.

EARLY DIAGNOSIS OF THE TUBERCULOUS KNEE JOINT IN EARLY CHILDHOOD. M. LANGE, Gaz. d. hôp. **105**:716 (May 11) 1932.

Describing the symptoms of tuberculous knee-joint, Lange emphasizes the fact that the elongation of the involved limb is noticed much earlier than in syphilis.

Roentgen examination of the knee-joint, in which very soft rays are used, is important in early diagnosis, as it will show the fungoid synovial membrane, while the fluid in syphilitic hydarthrosis will admit the rays.

KAJDI, Baltimore.

TUBERCULOUS ALLERGY AND IMMUNITY. J. HEIMBECK, Presse méd. **40**:528 (April 6) 1932.

B C G vaccination has been practiced in the Municipal Hospital of Oslo since 1927. Those patients who had given a negative reaction to the Pirquet test on vaccination showed local reactions varying from abscess to a slight local induration or no reaction at all; that is, some patients after vaccination gave a positive reaction to the Pirquet test, while others continued to give a negative reaction. The B C G used gave widely varying results, with a number of possible explanations. The age of the culture seemed to have more bearing on results than any other single factor. B C G, then, must be regarded, not as certain means of immunization, but as a feeble virus with variable immunizing effect, capable of producing, under certain conditions, the allergy demonstrable as a positive reaction to the Pirquet test.

BIEKER, St. Petersburg, Fla.

THE UNDERLYING PATHOLOGIC ANATOMY AND BACTERIOLOGY OF TUBERCULOUS RHEUMATISM. F. BEZANÇON, M. WEIL, J. DELARUE AND V. OUMANSKY, Presse méd. **40**:641 (April 27) 1932.

A report of a case is given, with pathologic findings. A woman, 31 years of age, had for five years very painful multiple arthritis, subacute and febrile, with no hydrarthrosis. Her mother and sister were tuberculous. The patient had pleurisy at the age of 13, and hemoptysis at 19, which persisted for seven years at infrequent intervals. There were respiratory changes and discrete opacities in the apexes of both lungs. Tubercle bacilli were demonstrated in the sputum by inoculation of guinea-pigs. Pericarditis with effusion caused death. Pathologic study showed that the articular capsules were thickened and hardened. the synovial membranes were avascular with fibrous bands, and there were adhesions between the capsule and the articular surfaces. There was no caseation or miliary tubercles. Perivascular infiltration with polymorphonuclears, lymphocytes and plasma cells constituted the typical lesion. Tubercle bacilli were demonstrated in some of the nodules. Inoculation of guinea-pigs with material from the synovial surfaces gave positive results. There was cellular infiltrations in the portal spaces and the malpighian bodies. The lungs contained sclerotic nodules. There were cellular infiltrations in the pericardium and in all the viscera.

In most cases, tuberculous arthritis may be considered the result of a bacillary septicemia with localization in the synovial surfaces, producing acute arthritis and hydrarthrosis ("white swelling"). It occurs in young persons, apparently as the result of hypersensitiveness, and may be a type of allergic reaction. It rarely exists in persons with pulmonary tuberculosis. Poncet's theory as to the relation between tuberculosis and arthritis deformans seems rather far-fetched, the latter being a trophoneurosis rather than a chronic infection.

BIEKER, St. Petersburg, Fla.

MALIGNANT LYMPHOGRANULOMA AND TUBERCULOSIS. F. BEZANÇON, WEISMANN-NETTER, R. OUMANSKY AND DELARUE, Presse méd. **40**:693 (April 30) 1932.

Six cases of lymphogranuloma are reported, in an attempt to discover any possible relationship to tuberculosis. In three cases there was no trace of tuberculosis. Biopsy of the cervical glands gave negative results histologically, no bacilli were found, inoculation of guinea-pigs gave negative results and tuberculin reactions were negative. In three other cases with the same typical findings of multiple adenopathies, eosinophilia, pruritus and fever, the coexistence of tuberculosis could be definitely established. These cases fall into three categories: (1) tuberculosis evidenced by positive inoculation of guinea-pigs with biopsy material which showed no histologic evidence of tuberculosis; (2) tuberculosis shown by positive results of inoculation with autopsy material showing no histologic evidence of the disease; (3) positive results of inoculation with miliary tuberculosis demonstrated at autopsy. The coexistence of tuberculosis may be partly explained by the frequency of its development in any chronic disease. It may be that an anergy is provoked by the evolution of the lymphogranulomatosis, since the tuberculin reaction usually disappears during the course of the disease. There seems to be no evidence that the bacillus of Koch influences the development of lymphogranulomatosis, although tuberculosis may coexist independently of the other disease. All attempts to produce granulomatosis experimentally by injection of tubercle bacilli have failed.

BIEKER, St. Petersburg, Fla.

FIVE YEARS OF VACCINATION WITH B C G AT LA ROCHELLE. M. LANCELOT, Presse méd. **40**:837 (May 25) 1932.

Lancelot comments on the unfortunate effect of the Lübeck tragedy and on the attitude of the public and of the profession toward vaccination with B C G. While every one familiar with B C G knows that it is harmless, there is an increasing hesitation about its use.

Figures from La Rochelle show that in the five years from Jan. 1, 1927, to December, 1931, there were 4,494 births; 1,800 persons were vaccinated. Of these, between birth and 1 year of age, 94 died, a mortality rate of 5.2 per cent. Of the 2,694 unvaccinated babies, 268 died in the first year, a mortality of 9.9 per cent, almost twice the mortality of the vaccinated group. The figures speak for themselves.

BIEKER, St. Petersburg, Fla.

A NEW SERIES OF OBSERVATIONS ON INFANTS WHO HAVE RECEIVED B C G AT BIRTH. P. NOBÉCOURT and R. LIÈGE, Rev. de la tuberc. **12**:62 (Oct.) 1931.

The authors give in detail their observations of seventeen infants previously vaccinated with B C G who were later admitted to the hospital suffering from a variety of conditions. Their ages varied from a few days to several months. Elsewhere they had reported a group of thirty-six similar cases, and in this paper summarize their findings in the entire series. Of the total fifty-three patients, nineteen gave a positive cutaneous reaction to tuberculin. In seven of the infants who gave positive reactions, evidence of localized tuberculosis was wholly lacking. In the remaining twelve infants there were clinical and roentgen evidences, which, if the patients had not received B C G, would have warranted a diagnosis of tuberculosis. Ten of the nineteen patients died. On a clinical basis alone it is difficult to draw any conclusions relative to the pathologic possibilities of B C G or to its value as a preventive agent. In those infants whose tuberculin reactions were negative, it was manifestly impossible to determine whether or not the vaccine had been absorbed or whether immunization had been successful. In infants with positive reactions, the facts revealed by clinical, laboratory and postmortem study have been variable and confusing. Some of the patients were clinically free from tuberculosis; in others were found tracheobronchial adenopathies, but whether these were due to the action of B C G or Koch's bacillus it was impossible to determine.

Commenting on these observations, Calmette suggests that the authors, in analyzing their cases, placed too much dependence on impressions and arrived at conclusions not yet warranted by the facts observed. He urges that impressions not be allowed to usurp the place of truth. In answer Nobécourt quotes from "L'Imitation," *"Nostra opinio et nostra sensus saepe nos fallunt,"* and asks "Where is truth?"

SMITH, Ogden, Utah.

REACTIONS OBTAINED WITH TUBERCULIN. HANS JACOB USTVEDT, Rev. de la tuberc. **13**:121 (Feb.) 1932.

The reaction to tuberculin is a specific reaction. It differs from nonspecific reactions in being more slow in its evolution. There is no reason to believe that negative reactions are encountered with notable frequency in persons with clinically cured tuberculosis. The technic of choice with the Pirquet test is by scarification, and the reaction should be read in forty-eight hours. An area of induration 2 mm. in diameter may be considered to indicate a positive reaction. Slighter reactions demand a repetition of the test. The Mantoux test should not be made with more than 1 mg. of tuberculin. The reaction should be read in seventy-two hours, when an infiltration of 10 mm. may be considered positive. The significance of lesser degrees of infiltration is not well understood and merits serious investigation. When the Mantoux test has been found to give results superior to those of the Pirquet, the author would attribute the results favorable to the former to technical deficiencies. When the Pirquet test is made with the proper technic and when nonspecific reactions are carefully differentiated from the positive Mantoux reaction, it is certain that the differences in the results between the two methods will tend to become effaced.

A critical study of the statistics from 1907 to 1914 relative to the frequency of positive reactions has convinced the author that the figures indicating an

unusually high incidence in early childhood give an exaggerated idea of the prevalence of the disease at this age. From his own researches he concludes that during the period from 1914 to 1930 there has been a real decline in the frequency of infection among children of school age, and especially in the younger age groups.

SMITH, Ogden, Utah.

ELIMINATION OF TUBERCLE BACILLI BY THE BILE IN TUBERCULOUS PATIENTS. C. CURRADO, Riv. di clin. pediat. **30**:46 (Jan.) 1932.

The author examined for tubercle bacilli the duodenal contents and the stools of twenty-five tuberculous children in whose sputums no tubercle bacilli were found microscopically. The duodenal contents were obtained by an Einhorn tube.

Only three times in the bile and five times in the stools were tubercle bacilli found; in each case the child was expectorating.

The author believes that the biliary route is a rare one for the elimination of tubercle bacilli, and certainly of minimal practical importance diagnostically and therapeutically.

HIGGINS, Boston.

PHLYCTENULAR CONJUNCTIVITIS AND TUBERCULOSIS. M. TEJEDA, Arch. de oftal. hispano-am. **32**:219 (April) 1932.

The author does not consider a relation between phlyctenular conjunctivitis and tuberculosis as settled. The great frequency of a positive tuberculin reaction in the former is not conclusive.

In this paper he considers a hundred cases of phlyctenular ophthalmia studied in relation to tuberculosis from the standpoints of their history, clinical symptoms, reaction to tuberculin and roentgen examination. As regards the history, in twenty cases the existence of an infecting focus in the patient was demonstrated. As regards the clinical manifestations, eighteen presented symptoms of tuberculosis, fifteen being scrofulous. A positive tuberculin reaction (Pirquet-Mantoux) was found in eighty-six cases. Eighteen patients showed positive lesions by roentgen examination. The author found fourteen cases with a negative tuberculin reaction, one of which he reports in detail in which no clinical relation to tuberculosis could be demonstrated.

He considers that, apart from local applications, general treatment of possible coexisting tuberculous and focal lesions is important.

FINLAY, Havana, Cuba. [ARCH. OPHTH.]

PHRENECTOMY AND PULMONARY TUBERCULOSIS OF THE CHILD. P. CANTONNET BLANCH, Arch. de pediat. d. Uruguay **3**:53 (Feb.) 1932.

Phrenectomy is a collapse therapy method that can be applied to the child and that under certain circumstances may give brilliant results. Success depends on determining the proper indication for the procedure and avoiding exaggerated claims that tend only to discredit the method. Phrenectomy should not be employed in complete unilateral tuberculosis.

The correct amount of lung retraction promises the best results. Not all of such processes are benefited, however, by the method. The procedure is contraindicated in caseating, ulcerating lesions. The best results are obtained from phrenectomy when the right upper lobes are involved.

Isolated caverns in otherwise healthy pulmonary tissue are no contraindication for the use of the procedure. Phrenectomy may be performed alone or may be combined with pneumothorax or thoracoplasty.

SCHLUTZ, Chicago.

CLINICAL RESULTS WITH THE SAUERBRUCH-HERRMANNSDORFER-GERSON DIET IN TUBERCULOSIS. FRANZISKA BOLDT, Arch. f. Kinderh. **94**:293 (Oct. 23) 1931.

Seventeen children with pulmonary tuberculosis, already under observation in the hospital, were placed for a period of about six months on the Sauerbruch-

Herrmannsdorfer-Gerson diet. On examination of the lungs eight children showed an improvement, and nine remained about the same or became worse. The sedimentation test varied considerably and could not be correlated with clinical progress, nor was there any change in the appearance of the scrofulous lesions. The children gained in height and weight, but that would be expected with any adequate diet. Intercurrent infections were no fewer than usual. The authors feel that no particular benefit is derived from the diet, and they have abandoned it.

LESLIE, Evanston, Ill.

THE FREQUENCY OF TUBERCULOUS INFECTION IN CHILDREN AS SEEN IN PRIVATE PRACTICE. H. BRÜNING, Arch. f. Kinderh. **95**:162 (Feb. 5) 1932.

From a study of statistics showing the incidence of positive tuberculin reactions in infants and children seen in private practice at different times during the past twenty years, it appears that there has been very little change in the frequency with which infection with the tubercle bacillus occurs. The incidence is about 5 per cent in infants, 10 per cent in small children, 25 per cent in young school children and 40 per cent in older school children.

LESLIE, Evanston.

THE PROGNOSIS OF PULMONARY TUBERCULOSIS IN CHILDREN. K. HASSMAN, Arch. f. Kinderh. **96**:193 (June 3) 1932.

Eighty children admitted between 1919 and 1927 to the University Pediatric Department at Graz because of active pulmonary tuberculosis were studied in 1929 from the standpoint of prognosis as affected by age and sex. The total mortality was 28.7 per cent. The highest mortality was found in infants under 2 years of age and in children at the age of puberty. There was a slightly larger number of girls than boys in the series, and the mortality for girls was slightly higher. Of the fifty-seven children still living in 1929 only five were considered completely cured; in 24 others the process was inactive, but they still showed evidence of tuberculosis in the lungs on roentgen or physical examination.

LEMASTER, Evanston, Ill.

EXAMINATION OF URINE OF CHILDREN ON THE SAUERBRUCH-HERMANNSDORFER-GERSON DIET. JOSEH CSAPO, MARIA PÉTERFY and ELLA PÁLFY, Arch. f. Kinderh. **96**:231 (June 3) 1932.

Quantitative urinalyses were made for three weeks on six tuberculous children receiving the Sauerbruch-Hermannsdorfer-Gerson diet with cod liver oil, but no minerals. Preceding and subsequent control periods were conducted on a normal diet. No noteworthy changes were recorded in the daily determinations of volume, specific gravity, creatinine, phosphate, sulphate, organic acids or total nitrogen. However, on this diet there was a decided decrease in the chlorides, total acids, fixed base, total base and ammonia percentage. The authors conclude that if the diet has any effect on the acid-base balance, it causes a slight tendency toward the alkaline side.

LEMASTER, Evanston, Ill.

REPLY TO DIETL'S REMARKS. B. EPSTEIN, Arch. f. Kinderh. **96**:235 (June 3) 1932.

Dietl interpreted a previous publication of Epstein as minimizing the importance of tuberculin tests and roentgen examination in children suspected of having tuberculosis. Epstein replies that he does not discourage these procedures, but does emphasize the value of the history and of clinical examination in the early diagnosis, prognosis, pathologic study and management of tuberculosis.

LEMASTER, Evanston, Ill.

CLINICAL SIGNIFICANCE OF THE DEMONSTRATION OF TUBERCLE BACILLI IN THE BLOOD STREAM. LUDWIG POPPER, Deutsche med. Wchnschr. **58**:89 (Jan. 15) 1932.

Popper examined the blood of one hundred patients, using the Löwenstein method, in order to demonstrate tubercle bacilli in the blood stream.

In 17 per cent of seventeen tuberculous patients he obtained positive results. Fifteen per cent of the forty-four rheumatic patients also gave positive blood cultures. The greatest percentage, i. e., 23 per cent positive results, occurred among forty-nine patients with heterogeneous diagnoses, grip, sepsis and other diseases. Popper interprets these results by the hypothesis that acute febrile conditions reactivate latent tuberculosis, the manifestation of which is the presence of tubercle bacilli in the blood stream. That few of the patients die of tuberculosis he explains by some unknown, possibly immunologic reason.

KERESZTURI, New York.

IS THERE TUBERCLE BACILLEMIA IN TUBERCULOSIS OF THE SKIN? FRANZ KOCH, Deutsche med. Wchnschr. **58**:90 (Jan. 15) 1932.

The author repeated Löwenstein's work by examining the blood of twenty-five patients for tubercle bacilli. These patients were suffering from different forms of tuberculosis of the skin or from tuberculous epidydimitis. All the cultures turned out to be negative for tubercle bacilli. However, the Löwenstein culture medium was a very good one for the growth of tubercle bacilli obtained from the sputum of patients with definitely open tuberculosis.

KERESZTURI, New York.

TREATMENT OF PATIENTS WITH LUPUS. SIGWALD BOMMER, Deutsche med. Wchnschr. **58**:91 (Jan. 15) 1932.

The Sauerbruch-Herrmannsdorfer diet, as used by many workers, has proved to be of great therapeutic value in the treatment of tuberculosis of the skin. The principle of this diet is salt restriction, meat limitation and a rich vitamin and fat supply.

Bommer thinks that the good effect of this diet affects the capillary walls by equilibrating the water exchange between blood and tissues, in this way influencing indirectly the inflammatory processes.

The only drawback of this diet is the tastelessness of the food due to the withdrawal of the salts. Therefore, Bommer tried a salt mixture balanced so that the chloride anion is replaced and counterbalanced by other anions. He used the Sauerbruch-Herrmannsdorfer diet with this mixture in thirty-three patients with lupus with just as good results as the original salt-free Sauerbruch diet could have given.

KERESZTURI, New York.

THE DIAGNOSIS OF ACTIVE TUBERCULOSIS. KARL G. HEYMANN and ELLEN NUSSBAUM, Monatschr. f. Kinderh. **53**:301, 1932.

Leuchtenberger and Lorenz, in the Cologne Children's Clinic, attempted a new method for the diagnosis of active tuberculosis, through serologic means. Their technic differed from the usual complement reactions in that they believed that the blood of a patient with active tuberculosis contained increased hemolysins against sheep's blood corpuscles.

The writers examined blood serums in fifty-five cases of clinical tuberculosis as well as many controls. They conclude that the new method is not advisable for children in that it requires 15 cc. of blood. They also do not believe that the method is of definite value in determining the activity of the process, though it does seem specific for a tuberculous infection.

GERSTLEY, Chicago.

THE SEROLOGIC DEMONSTRATION OF ACTIVE TUBERCULOSIS. M. WEICHSEL, Monatschr. f. Kinderh. **53**:390, 1932.

The writer refers to an article by Klinke and Hensel, who claimed to have a method for the diagnosis of active tuberculosis, based on serologic technic. The writers tested fifty-one serums of tuberculous children with this procedure and found that it was entirely unreliable compared with clinical examination.

GERSTLEY, Chicago.

CALMETTE PROPHYLAXIS AND THE ILLNESS OF THE LÜBECK INFANTS. R. KIMLA, Časop. lék. česk. **69**:1137 (Aug. 1) 1930.

The author reviews the Lübeck catastrophe and cites various authors on the question of the virulence of B C G. In France and Mexico, 573 children were inoculated with the same strain used in Lübeck, with no ill effects. Kirchner stated that more work must be done to settle the following questions: Whether B C G acts and remains as a fixed virus; whether B C G may become virulent under certain physiologic conditions; whether B C G actually propagates in the host, and whether there is a latent period after which B C G may become virulent. The author cultivated B C G in the conjunctival sac of rabbits for a period of two and a half years (twenty passages), and the B C G remained unchanged. A peculiar result is reported, however, after the inoculation of 0.001 mg. of B C G into the conjunctival sac of a guinea-pig. The local reaction healed in four months, and then after intensive therapy with tuberculin injected subcutaneously had been given, autopsy revealed generalized tuberculosis. Some authors are tempted to use B C G only in infants exposed to an environment of tuberculosis and not in absolutely healthy infants with no focus of contamination.

STULIK, Chicago.

ATYPICAL TUBERCULOUS MENINGITIS. P. BUTLER, Hygiea **94**:209 (March 31) 1932.

In nineteen cases cited by Butler, tuberculous meningitis had at some stage simulated or caused confusion with cerebellar tumor, cerebral abscess together with chronic otitis, compression myelitis, sarcomatosis of the cerebral meninges, acute polyarthritis with transient paralysis of the bladder, epidemic meningitis and poliomyelitis in the preparetic stage. He says that the focal symptoms usually appear after meningeal signs have set in, unless the focal symptoms dominate the clinical picture. The phenomena of focal deficiency may, however, constitute the initial symptoms, and a longer or shorter period may elapse before the symptoms proper of meningitis appear. With a fever-producing tuberculous process in other organs, rapidly supervening focal symptoms from the central nervous system may be the first sign of meningitis.

ELGHAMMAR, Chicago.

## Internal Diseases

ROENTGENOLOGIC DIAGNOSIS OF DISEASES OF THE UPPER RESPIRATORY TRACT IN CHILDREN. HENRY K. PANCOAST and EUGENE P. PENDERGRASS, Am. J. Roentgenol. **23**:241 (March) 1930.

Roentgenologic studies of the chests of infants and children should always include the neck, in order to detect possible obstructive lesions in the upper respiratory tract that may explain, in part or entirely, suspected intrathoracic conditions. The basis for the detection of conditions in the upper respiratory tract is complex. The soft tissues of the neck surround a more or less rigid, air-containing passage, the pharynx, larynx and trachea, which can be visibly encroached on; a collapsed potential space, the esophagus, can be filled by opaque mediums; the dense vertebrae occupy a fixed relative position for estimating displacements and making measurements; clear views of the intrathoracic trachea

and its relations are easily obtainable, and certain phenomena observable in the chest may be associated with or due to obstructions in the upper air passages.

The following structures are easily seen in roentgenograms of the neck at ages when their detection is important: the posterior border of the tongue, uvula, pharyngeal cavity and its walls, epiglottis, aryepiglottic folds, pyriform sinuses, laryngeal vestibule, ventricular and vocal folds, laryngeal ventricles and the lower limits of the laryngeal cavity. A detailed discussion of conditions amenable to roentgen diagnosis includes streptococcus laryngitis, acute diphtheria, postdiphtheritic and other forms of stenosis, tuberculous adenitis with calcifications, retropharyngeal and retrotracheal abscess, encroachments on the nasopharynx, foreign bodies and enlarged thymus. The only definite or reliable signs of an enlarged or potentially obstructive thymus are narrowing of the trachea at the upper thoracic outlet on inspiration, too great a collapse on expiration or buckling at either phase, as shown in the lateral view, or lateral deviation of the trachea, as shown in the sagittal view. In the differential diagnosis of obstructive phenomena or persistence of symptoms after irradiation, the following must not be forgotten: foreign bodies, retropharyngeal abscess, tracheal and laryngeal stenosis, recurrent laryngeal paralysis from the thymus, the relaxed soft tissues of the pharynx and larynx in the young, asthma, whooping cough, meningitis and congenital cardiac conditions. This article is presented as a preliminary report.

STULIK, Chicago.

SOME OF THE DEFORMING BONE DISEASES OF ADOLESCENCE. A. L. GRAY, Am. J. Roentgenol. **23**:485 (May) 1930.

The author discusses Calvé's or Scheuermann's disease, separation of the head of the epiphysis of the femur (slipping epiphysis), osteochondritis deformans juvenilis coxae (Legg-Perthes' disease), apophysitis of the anterior tibial tubercle (Osgood-Schlatter disease) and osteochondritis of the scaphoid (Kohler's disease). It seems that in all of these conditions the immediate cause of the deformity resulting from the changes of the bones is a deficient blood supply, which may be caused by traumatism, infection involving the blood supply or, usually, both of these factors in a greater or less degree. Osteochondritis or epiphysitis may involve the adolescent bone in any locality; however, it is most frequent in those localities where greater stress is borne.

STULIK, Chicago.

OSTEITIS FIBROSA CYSTICA OF THE SKULL ASSOCIATED WITH HEMIANOPIA AND PSYCHOTIC SYMPTOMS. HAROLD D. PALMER, REED HARROW and LOUIS A. SCHWARTZ, Arch. Neurol. & Psychiat. **27**:45 (Jan.) 1932.

A case of osteitis fibrosa cystica in a 14 year old girl was reported. She sustained a fracture of the occipital bone at 26 months of age. Change of personality was noted at 9 years which assumed "psychotic proportions" at 12 years. The mental symptoms became so pronounced that she was confined to a psychiatric institution. She had headache, apathy and dream states, heard voices and had visual hallucinations. There was a marked suicidal trend. There was a left homonymous hemianopia. A roentgenogram showed a large cranial defect of the occipital bone. A hollow bony cyst was found at operation. The inner wall was bulging, compressing the brain and accounting for the visual hallucinations and visual defect. There was marked improvement after the operation.

BEVERLY, Chicago.

LEAD POISONING IN CHILDREN: THE CEREBRAL MANIFESTATIONS. CHARLES F. MCKHANN, Arch. Neurol. & Psychiat. **27**:294 (Feb.) 1932.

Early manifestations of lead poisoning are anorexia, constipation and colic associated with anemia. More serious symptoms are vomiting (often projectile), a slow pulse, visual disturbances, delirium, stupor, coma or convulsions. Often there are elevation of blood pressure, choked disk and separation of the cranial

sutures. Death is due to respiratory failure. The neural symptoms are due to cerebral edema. If the patient survives, there may be sequelae in the form of blindness, spasticity and mental deficiency due to cerebral atrophy secondary to anemia resulting from the cerebral edema.

There may be a lead line at the margin of the gums, stippling of red blood cells, an increased percentage of reticulated red blood cells and dense broad bands at the ends of the long bones. The last mentioned change is due to the deposition of lead and may be present with decreased calcium content of the bones. Lead may be found in the urine and an increased amount in the stools. Lead may be seen in x-ray films of the abdomen as opaque areas, presumably unabsorbed lead in the gastro-intestinal tract.

Treatment consists in relieving the cerebral edema by decompression and the use of magnesium sulphate given intramuscularly. The author feels that decompression should be considered in severe cases. Parathyroid hormone has been used. The use of cod liver oil and calcium is indicated.

A case occurring in a child of 22 months with resulting unilateral convulsions and hemiparesis is reported. Encephalograms showed extensive cortical atrophy.

BEVERLY, Chicago.

CHLORO-ERYTHROBLASTOMA. NELSON J. HOWARD and JAMES B. MCNAUGHT, Arch. Path. **13**:56 (Jan.) 1932.

A rapidly growing tumor was removed from the upper nasal quadrant of the left orbit of a girl 6 years old. The tumor was 3.5 by 3 by 1.5 cm. and olive green. The cell most frequently encountered corresponded to the myeloblast of the bone marrow; there were also numerous myelocytes and some polymorphonuclear cells. Megaloblasts and other cells of the erythrocytic series were found scattered throughout the tumor. Examination of the peripheral blood one week after operation showed: 8 per cent myelocytes, 3.3 per cent myeloblasts and 2 megaloblasts; the white cell count was 21,050. Biweekly treatments with deep roentgenotherapy were instituted, but the child continued to become worse, showing progressive anemia, thrombopenia and symptomatic purpura. Death occurred after two and one-half months. Tumors similar to the original one were found associated with various bones throughout the body.

The presence of erythroblasts and myeloblasts in the same tumor seem to support the monophyletic theory of the origin of blood cells, although no parent stem cell could be identified.

LESLIE, Evanston, Ill.

THE GROWTH HORMONE: REPORT OF A CASE OF JUVENILE HYPOPITUITARISM TREATED WITH EVANS' GROWTH HORMONE. WILLIAM ENGELBACH, Endocrinology **16**:1 (Jan.) 1932.

With the exception of the rare occurrence of pituitary tumor, perusal of the literature does not reveal a description of pituitary disorder during the early years of life. Yet both deficiency and hyperactivity of the anteropituitary are prevalent in infancy and juvenility. The hormone originating in the eosinophilic cells of this lobe must be supplied in large amounts during infancy since somatic growth depends largely on it. During the past year and a half eight cases of pure infantile pituitarism have been found, all in patients under 5 years of age, falling into the following classification: (1) anterior lobe pituitarism, (*a*) hypopituitarism, five cases, and (*b*) hyperpituitarism, one case; (2) adiposogenital pituitarism, two cases; (3) pituitary tumor.

Deficiency of the anterior lobe during the early years of infancy must be inherited. Proof of this depends on a familial history of pituitarism or lack of pituitary response during gravidity, at which time the embryonic hypophysis is being evolved. Of the eight patients six had a history of parental or familial endocrinopathies.

A table is given recording minimal and maximal measurements for normal infants from birth to 20 months of age. Any deviation below the minimum or above the maximum indicates insufficiency or oversupply of the growth hormone, provided all other causes for abnormal growth can be excluded.

The diagnosis of hypopituitarism is easily made by a process of elimination. Hypothyroidism is excluded by lack of retardation of the osseous centers, mental defects, orthodontial and other general signs. (In the late juvenile years a secondary osseous retardation is present in the pituitary deficiency. This is due to the secondary hypothyroidism caused by the lack of growth hormone supplied to the thyroid gland.) No other endocrine disorder causes the degree of microsomia present in hypopituitarism. Deficiency diseases, chronic infections and congenital heart disease must be ruled out.

The case of a 3 year old child with unusually small measurements is recorded. Except for the small stature, the patient was relatively normal. Roentgenograms revealed normal development of the epiphyseal centers.

A second case in a child of 9 years of miniature stature, the size of an average 3½ year child, is described. There had been practically no growth since the age of 6. Evans' growth hormone was given intramuscularly in daily doses gradually increased to 10 cc. During the nine months that it was administered the child's height increased 2.7 inches (6.85 cm.); the weight, 7.5 pounds (3,400 Gm.), and other measurements in proportion.

This patient was the first human being to be treated with Evans' growth hormone, which is the best preparation to use. Until this preparation is generally available other alkaline extracts of the anterior hypophysis may be substituted, such as an anterior lobe pituitary preparation that has from one-third to one-half the potency of Evans' hormone. Preparations given orally are probably ineffective.

JACOBSEN, Buffalo.

THE CLINICAL VALUE OF THE SCHILLING BLOOD COUNT. ROY R. KRACKE, J. M. A. Georgia **20**:393 (Oct.) 1931.

The principle and method of making the Schilling differential count are reviewed. The application of the index is shown by sample counts illustrating the three phases occurring in an acute infectious disease. The diagnostic and prognostic value of the Schilling differential count is discussed in connection with four cases.

KISER, JR., Atlanta, Ga.

RECENT ADVANCES IN THE PREVENTION AND TREATMENT OF DISEASES IN CHILDREN. JOSEPH YAMPOLSKY, J. M. A. Georgia **20**:423 (Nov.) 1931.

1. Diphtheria. The author discusses various methods of immunization, including toxin-antitoxin, toxoid and the percutaneous method of Loewenstein.

2. Syphilis. The author tells his own method of treating syphilitic infants, which is the administration of a solution of neoarsphenamine, 0.1 Gm. per 15 pounds (7 Kg.), alternated with mercurosal, 0.5 grain (0.03 Gm.) per 30 pounds (14 Kg.). Injections are made into the peritoneal cavity. Sixteen weekly injections constitute a course, two such courses being required during the first year of life. Twenty-six cases in which the author's method was used are discussed.

3. Scarlet fever. The use of antitoxin and active immunization in scarlet fever is discussed.

4. Measles. The author reviews the use of convalescent serum, emphasizing the advantage of obtaining a mild attack of measles and consequent permanent immunity.

5. Anemia. The use of copper and iron in the treatment of nutritional anemia is discussed.

6. Rickets. Viosterol, cod liver oil and sunlight in the treatment of rickets are reviewed.

TULAREMIA STUDIES IN GEORGIA. JOSEPH C. MASSEE, J. M. A. Georgia **21**:7 (Jan.) 1932.

During a period of sixteen months, ending in April, 1931, sixty-six cases of tularemia were diagnosed by the laboratories of the Georgia State Board of Health. Fulton County, with sixteen cases, had the largest number of cases for any county. These occurred chiefly in market workers who handled rabbits. Data are given on thirty-five cases, in which there were two deaths. The ulcero-glandular type of tularemia was the most predominant; tularemia accompanied by pneumonia occurred in two cases. The importance of tularemia in the differential diagnosis of other diseases is stressed. KISER, JR., Atlanta, Ga.

TREATMENT OF BRONCHOPNEUMONIA IN INFANCY. G. PAISSEAU, Union méd. du Canada **61**:578 (April) 1932.

*Prophylaxis.*—It is possible to prevent, in a certain measure, the appearance of bronchopneumonia in the course of infectious diseases in infancy. In principle, the prophylaxis of bronchopneumonia is essentially hygienic, and no serotherapy or vaccine therapy has shown proof of its efficacy. The patient should be kept in a room at a temperature of 17 C. It is useful to maintain constantly in the room boiling water to which have been added one or two eucalyptus leaves.

*Symptomatic Treatment.*—Every three or four hours, according to the severity of the case and as long as the temperature is 38.5 or 39 C. (101 to 102 F.), the patient's thorax and trunk should be enveloped in a wet pack wrung out of water at from 20 to 25 C. for from one-half to one hour. Simple mustard plasters are of value in bronchitis, but in long-continued bronchopneumonia their irritation is apt to interfere with the packs. As a stimulant remedy, ammonium acetate, and in depression, camphor in oil hypodermically or strychnine sulphate should be given.

In dyspnea or cyanosis oxygen inhalations through an oxygen chamber or mask should be given.

Polyvalent antipneumococcic serum, antistreptococcic serum and antidiphtheritic serum have been employed, but should not be depended on alone. They may be joined with vaccine therapy by stock polyvalent vaccines containing Pneumococcus, Streptococcus, Enterococcus, Staphylococcus, Pfeiffer's bacillus, Friedländer's bacillus, Bacillus pyocyaneus and other organisms. It is recommended that one pursue the vaccine treatment until the patient is afebrile, but not more than six to eight injections, at one or two day intervals, should be given if no good results appear. Intramuscular injections of a colloidal gold preparation in large doses have a favorable effect on the temperature curve.

In very grave cases one ought to consider the production of a fixation abscess.

DRAKE, Toronto, Canada.

SOME FACTORS IN THE CAUSATION OF HYDRONEPHROSIS. J. P. HOSFORD, Lancet **1**:435 (Feb. 27) 1932.

It is best to confine the term congenital to the types of hydronephrosis that are present in the new-born or are discovered soon after birth. They fall into two groups: (1) cases with some discoverable mechanical cause obstructing either the ureter or urethra, and (2) cases of megalo-ureter combined with hydronephrosis in which there is no discoverable obstruction.

Acquired hydronephrosis may also be divided into two groups: (1) cases in which there is a demonstrable macroscopic obstruction, and (2) those in which there is no obstruction.

Some of the causes put forward to explain the occurrence of the so-called idiopathic type of hydronephrosis include: (1) stricture of the ureter; (2) abdominal mobility of the kidney; (3) aberrant renal vessels, and (4) folds and valves.

"Therefore, in an endeavor to suggest a cause for this condition of hydronephrosis, it seems to be necessary to attribute it to some disturbance of the neuro-muscular mechanism, mainly because there is no other explanation to

account either for the special dilatation of the pelvis or for the presence of dilatation, in some cases, without mechanical obstruction. And it is believed that the various causes which have been or are put forward from time to time are secondary to the hydronephrosis and not the primary cause." LANGMANN, New York.

METHENAMINE IN THE TREATMENT OF ENURESIS. LEOPOLDO ROSSI, Clin. pediat. **14**:34 (Jan.) 1932.

The various theories concerning the pathology as well as the various therapeutic methods in the treatment of enuresis are reviewed. In a series of fifteen cases of enuresis in children, which had failed to respond to any form of treatment, the author gave subcutaneous injections of methenamine, U. S. P. He used a solution in distilled water (25 cg. in 2 cc.), and repeated the injection every third day. His results were uniform, with clinical cure in thirteen of his cases; the two remaining patients failed to respond in any degree. The author believes that this is a practical and convenient method of treatment which should be attempted in all obstinate cases of enuresis that do not respond to the usual methods.

SIGNORELLI, New Orleans.

CONTRACTED KIDNEYS IN CHILDHOOD. M. KLEIN, Frankfurt. Ztschr. f. Path. **41**:317, 1931.

The author describes one case of malignant nephrosclerosis and two cases of chronic glomerulonephritis (secondary contracted kidneys) occurring in children. A short review of reported cases of malignant nephrosclerosis is also given. The differences between the two types of kidneys are discussed. In cases of malignant nephrosclerosis, endarteritis and periarteritic changes combined with necrosis of the walls of the arterioles are found. These changes extend into the vasa afferentia and capillaries of the glomeruli. In cases of chronic glomerulonephritis, blood vessel changes may be present, but endarteritis and arterionecrosis are not characteristic. In cases of malignant nephrosclerosis, inflammatory changes within the glomeruli may be the result of primary inflammatory changes of the blood vessels. The inflammatory changes of the glomeruli are not so severe and diffuse as in cases of chronic glomerulonephritis. The arteriosclerosis leads to disappearance of glomeruli, without accompanying inflammatory changes of the glomerulus. Malignant nephrosclerosis does not occur secondary to "nephrocirrhosis arteriosclerotica." The author believes that there are only nine proved cases of malignant nephrosclerosis in children on record, while twenty-four cases that have been reported to be such are doubtful. Chronic inflammatory contracted kidneys (chronic glomerulonephritis) in children was found described in the literature twenty-two times. The blood vessel changes that are found in the spleen, liver, pancreas, brain, thymus and suprarenal glands are not inflammatory. Morphologically, they resemble the changes seen in arteriosclerosis. They probably are the result of the increased pressure occurring in renal insufficiency.

SAPHIR, Chicago. [ARCH. PATH.]

METHODS OF EXAMINATION IN THE CARDIOVASCULAR DISTURBANCES OF THE SCHOOL CHILD. L. DOXIADES, Gesundhfürs. f. d. Kindesalt. **6**:280 (Sept.) 1931.

The author still believes that it is possible to study the cardiovascular system by means of the so-called functional tests. REICHLE, Cleveland.

ALKAPTONURIA IN AN INFANT. KURT BALLOWITZ, Jahrb. f. Kinderh. **134**:182 (Jan.) 1932.

A rachitic infant 11 months old, whose diapers were stained brown, was found to excrete daily from 1.76 to 2.51 Gm. of homogentisic acid. No other anomalies were observed. CLAUSEN, Rochester, N. Y.

A Case of Generalized Xanthomatosis (Schüller-Christian Disease). Rudolf Attig, Jahrb. f. Kinderh. **134**:184 (Jan.) 1932.

The author gives a full clinical description of a typical case beginning in a boy at the age of 2 years and leading to death at 3½ years. The membranous bones and the dura mater were invaded by the tumors, which contained foam cells laden with doubly refracting lipoids.

Clausen, Rochester, N. Y.

Renal Infantilism. W. Mikulowski, Jahrb. f. Kinderh. **134**:205 (Jan.) 1932.

The author discusses the literature and presents the case of a boy aged 10 years, intelligent and active, who for four years had had hematuria and albuminuria, with urine of low fixed specific gravity, and the bodily and skeletal development of a boy of 6 years.

Clausen, Rochester, N. Y.

Symptomatology and Treatment of Pneumonia in Infants. R. Grosser, Kinderärztl. Praxis **2**:212 (May) 1931.

Pneumonia in infants is divided into the milder localized forms and the more severe septic-toxic pneumonias. The author offers nothing new in treatment except to emphasize the value of "sugar days," recommended by L. F. Meyer and Nassau. Since a high carbohydrate diet leads to alimentary disturbance only when given in combination with other foods, on certain days a 12 per cent dextrose solution is the only food given.

Huenekens, Minneapolis.

Progress in the Field of Diseases of Bones, Muscles and Joints. Siegfried Simon, Kinderärztl. Praxis **2**:446 (Oct.) 1931.

This paper gives an excellent review. It should be read in the original.

Huenekens, Minneapolis.

The Blood Pressure of Normal Infants and Children. Arthur F. Abt and Benjamin F. Feingold, Kinderärztl. Praxis **2**:516 (Nov.) 1931.

For infants the width of the arm band of the sphygmomanometer should be from 4 to 5 cm.; for older children, 9 cm. Sex, size, weight, age, the circumference of the arm, race, inheritance and climate definitely and regularly affect blood pressure. Less constant in their effects are the position of the patient, pulse rate, body temperature, meals, emotional disturbances, fatigue, movement and sleep. Infants at birth have an average systolic pressure of 55 mm. of mercury and a diastolic pressure of 40 mm., which gradually rises during the first ten days of life. Healthy children may sometimes have an astonishingly high systolic blood pressure (from 150 to 180 mm. of mercury), usually about the age of puberty.

Huenekens, Minneapolis.

Bang's Disease. L. R. Müller, München. med. Wchnschr. **78**:1813 (Oct. 23) 1931.

Müller describes several typical cases of undulant fever. The first case he observed was in himself. He had all the signs and symptoms, but agglutinins could not be found in the serum. The disease is most frequently mistaken for typhoid or paratyphoid. The cardinal symptoms are remittent fever with chilly sensations, slow pulse, headache, a clear sensorium, enlargement of the spleen and leukopenia. Erythema multiforme, aphthous stomatitis and a painless orchitis and epididymitis may occur.

Brahdy, Mount Vernon, N. Y.

Synthalin and Juvenile Diabetes. J. Procházka, Časop. lék. česk. **69**:606 (April 18) 1930.

The administration of synthalin (aminopentamethylenguanidine) was tried in eight cases of juvenile diabetes. Two children were unable to tolerate synthalin.

In one instance synthalin replaced insulin in the reaction on the blood sugar, but a resulting loss in weight necessitated a return to insulin. Three children were treated with synthalin alone for seven months without untoward effect. In two cases the amount of insulin was cut in half by using synthalin, but there was some loss in weight. Synthalin is not sufficient in itself for the treatment of diabetes of the advanced type. In early cases synthalin alone has some value, but usually only for a short period. In the combined treatment the saving in the amount of insulin and in the cost of medication is considerable.

STULIK, Chicago.

## Nervous Diseases

RESTLESSNESS IN INFANCY. JOHN CAREY, Illinois M. J. **61**:76 (Jan.) 1932.

In certain babies at birth, or shortly after birth, a hyperactive vagus associated with distention develops, owing to spasm of certain areas of the gastrointestinal canal, which produce pain and restlessness. Treatment consists of placing these children among placid surroundings, feeding them breast milk or a high protein diet and using atropine, phenobarbital or roentgen rays.

BARBOUR, Peoria, Ill.

POLIOMYELITIS: II. COMPARISON OF INTRAMUSCULAR INJECTION WITH COMBINED INTRASPINAL AND INTRAVENOUS INJECTION OF CONVALESCENT SERUM IN THE TREATMENT FOR EXPERIMENTAL POLIOMYELITIS IN MONKEYS. BEATRICE F. HOWITT, J. Infect. Dis. **50**:47 (Jan.) 1932.

The author's conclusion was: "In monkeys in the preparalytic stage the percentage of recovery from experimental poliomyelitis was greater when serum from convalescent monkeys was given intramuscularly than when it was administered by the combined intrathecal and intravenous method. Paralysis, however, was rarely prevented, and with one exception recovery was accompanied by varying degrees of atrophy of the affected muscles."

TOOMEY, Cleveland.

SURVEY OF ANTERIOR POLIOMYELITIS, AT GRASSLANDS HOSPITAL. B. C. HECHT, M. J. & Rec. **135**:19 (Jan. 6) 1932.

The author drew the following conclusions from a survey of the cases of anterior poliomyelitis at Grasslands Hospital. 1. The signs and symptoms of poliomyelitis in the epidemic of 1931 did not vary much in frequency of appearance from those in other epidemics. 2. There were few cases among the colored population, which may indicate a racial immunity. All suspected cases among Negroes should be particularly studied to rule out other conditions. 3. Early spinal taps should be performed in all suspected cases, especially during epidemic seasons. 4. The patients were generally robust healthy persons, but the author could not quite agree with Draper's description of the constitutional type necessary for the development of the disease. The incidence is greatest up to the age of 5 years. 5. The temperature is never alarmingly high, and does not play an important part in the disease picture as to prognosis or severity of the disease. 6. The cell count was generally below 200 cells per centimeter, but counts over 1,000 cells were observed. A high count offers a bad prognosis. 7. The efficacy of serum therapy cannot be scientifically judged unless control cases are used. However, individual cases give the clinical impression that the serum is of some value. 8. The mortality rate of true bulbar paralysis still remains about the same in spite of the use of the Drinker respirator. 9. In a certain number of cases paralysis develops in spite of serum treatment. 10. The follow-up of supposed abortive cases is just as important as treatment in cases of paralysis, since imbalance of intrinsic muscle groups is later exhibited in some of them, which leads to deformities.

WILLIAMSON, New Orleans.

THE CONVALESCENT STAGE OF POLIOMYELITIS: A SYNOPSIS OF TREATMENT. WALTER TURSLOW, M. J. & Rec. **135**:31 (Jan. 6) 1932.

This article contains a synopsis of treatment of poliomyelitis. The treatment is considered under two heads, protection and muscle reeducation, and after many months or even years of careful application of these principles, a reconstruction operation may be necessary. In conclusion, the author points out that the physician taking care of the convalescent from polyomyelitis must be patient, conscientious and optimistic; he must guard the patient against fatigue, and he must strive ever to prevent deformity. The convalescent stage may cover a long and tedious period, and the patient and the parents will need much encouragement, but the salvage is worth the effort, as many potential cripples are by careful management led into a condition of real efficiency.

WILLIAMSON, New Orleans.

CHOREA AND ITS TREATMENT. GABRIEL LAFRESNIÈRE, Union méd. du Canada **61**:589 (April) 1932.

The treatment of chorea is purely empiric, and all authors are in accord in giving preference to arsenical medication, particularly to arsenic trioxide, U. S. P. This last, administered by Weill's method, is believed to be the ideal medication, since it is the simplest and easiest preparation to use and the only one free from all toxicity. The dosage is 5 mg. per day at the start, increased by 5 mg. per day until a maximum of 40 mg. is reached. This dose is given for several days and then decreased by 5 mg. per day to zero. Each dose of arsenic is incorporated in 10 Gm. of butter and taken well spread on bread once a day during or at the end of a meal, but never during fasting.

DRAKE, Toronto, Canada.

PACHYMENINGITIS HAEMORRHAGICA INTERNA. J. GIBBENS, Proc. Roy. Soc. Med. **25**:129 (Dec.) 1931.

An infant of 11 weeks was admitted to the hospital because its head was slowly growing larger. The anterior fontanel was large and bulging. One cubic centimeter of spinal fluid was obtained by lumbar puncture under markedly diminished pressure, and 25 cc. of reddish-brown fluid by left ventricular puncture under marked pressure. Microscopic examination showed the Wassermann reaction of the blood to be negative. The Mantoux reaction was negative to 1 mg. Both fundi showed advanced choroidoretinitis. Three weeks after the report an abscess developed at the site of a subcutaneous injection of saline solution, and the child died shortly afterward from septicemia. At autopsy pachymeningitis haemorrhagica was not found, but there was a severe chronic internal hydrocephalus. The ventricles were filled with old hemorrhagic fluid.

WILLIAMSON, New Orleans.

TWO CASES OF FAMILIAL CEREBRAL DIPLEGIA WITH OPTIC ATROPHY. WILFRED SHELDON, Proc. Roy. Soc. Med. **25**:143 (Dec.) 1931.

The author reports two cases of this disease in the fifth and sixth children of a family of six. The other four siblings were normal. Neither child could stand or even sit up alone. Speech was defective. Both suffered from optic atrophy. There was rigidity of all the limbs. The Wassermann reaction in both was negative. Birth was normal in both children, so their condition cannot be attributed to birth injury. The etiology must be a matter of speculation.

WILLIAMSON, New Orleans.

SOME CONSIDERATIONS ON THE GENERAL ACTIVITY OF THE INFANT. D. SCHACHTER, Progrès méd., March 12, 1932, p. 461.

This is a discussion of the reflexes found in the new-born and in the older infant.

SANFORD, Chicago.

SOME TROUBLES ATTRIBUTABLE TO OCCULT SPINA BIFIDA. J. E. SAMSON, Union méd. du Canada **61**:386 (Feb.) 1932.

Occult spina bifida may bring about important trophic disturbances, prolonged enuresis and unexplainable painful phenomena. Motor, sensory and ataxic troubles sometimes make diagnosis troublesome and difficult; the well performed operation is without danger and renders a real service to the patient if the spina bifida is the only causal agent.

DRAKE, Toronto, Canada.

EARLY TREATMENT FOR POLIOMYELITIS BY SERUM FROM CONTACTS WHO ARE IMMUNE. H. GOUNELLE, Progrès méd., Nov. 28, 1931, p. 2169.

On the basis of the success obtained in giving serum from a recently vaccinated person to a youth of 21 years who was revaccinated and in whom encephalitis developed, the author advocates serum from immune contacts for poliomyelitis. Frequently, because of the scarcity of immune serum from old cases, actual cases are allowed to run too long to be certain of the diagnosis. With the method described any patient can be given serum, and the greater benefits obtained from early injection may be secured.

SANFORD, Chicago.

OPTIC PATHWAYS IN A CASE OF CONGENITAL ANOPHTHALMOS. A. SOUQUES and IVAN BERTRAND, Rev. neurol. **2**:1 (July) 1931.

The clinical aspects of this case were reported by Souques in 1915. The patient finally died of general sepsis following pyelitis. No vestige of a retina was found in the orbit. The orbital portion of the optic nerve was reduced to delicate filament, completely without medullated fibers and surrounded by a heavy sheath. The other nerves in the orbit were easily recognized, and the muscles appeared normal. The optic chiasm was formed by two delicate strands of tissue about the size of a normal trochlear nerve, and it contained no medullated nerve fibers. The optic tracts were much reduced, but Meynert's commissure was intact, although that of Gudden was not discerned. The external geniculate body was very small and malformed, small irregular cell groups being separated by considerable glial tissue and disappearance of the large ventral cells. The optic radiation was scarcely visible. The stratum sagittale internum (optic radiation of Gratiolet) was much reduced. The thalamus, including the pulvinar, was entirely intact, and the association fibers of the occipital lobe were partially undeveloped. The occipital cortex presented interesting modifications. The white line of Gennari was present but so poorly defined as to resemble the usual appearance of the medullated stratum of Baillarger. It lay deeper than usual and, microscopically, was found to be very thin. Most of the radial fibers above this had disappeared, while those below showed slight rarefaction. The tangential stratum of Exner appeared entirely normal. The striated cortex was reduced by one third, all strata being affected but particularly the deeper ones. Strata IVb and VIa were particularly dense, owing to the apposition of ganglion cells. Stratum IVb included numerous giant cells. The area striata presented a normal extent. The parastriate field was not notably affected.

The authors believe that in this case, although the condition occurred in two brothers of a family, an infectious process during early life caused the resorption of the optic vesicle, and that the structures directly dependent on this vesicle underwent complete atrophy, whereas those more or less distantly related to it showed less severe changes. This case, then, is not one of complete agenesis of the visual system.

FREEMAN, Washington, D. C. [ARCH. NEUROL. &. PSYCHIAT.]

MACROGENITOSOMIA PRAECOX ASSOCIATED WITH AN EPENDYMOGLIOMA OF THE MAMMILLARY REGION. G. HEUYER, J. LHERMITTE, DE MARTEL and C. VOGT, Rev. neurol. **2**:194 (Aug.) 1931.

A boy, aged 6 years, developed with abnormal rapidity and presented the physical appearance of a lad of 12. The sexual organs were especially well

developed, with a good growth of hair. The patient suffered from headache, which was worse on quick movements of the head; he walked a little gingerly, but he had never had any vomiting or convulsive seizures. The reflexes were active, with plantar extension on the left. There was no somnolence, glycosuria or polyuria. The cranial nerves were normal. Mentally, he appeared to be backward, and a mental age of 3 years had been reported. The sella turcica was small; the convolutional markings were visible in the roentgenogram. The spinal fluid escaped under increased pressure, but showed no abnormal elements. The epiphyseal region was explored without anything abnormal being found, and the child died two days after examination.

Serial sections through the region of the tuber cinereum showed a cystic tumor, apparently originating in the right mammillary body, causing slight compression of the surrounding structures, with dilatation of the aqueduct of Sylvius, but no evident pressure on the optic nerve. The epiphysis was entirely normal.

FREEMAN, Washington, D. C. [ARCH. NEUROL. &. PSYCHIAT.]

THE PATHOLOGIC ANATOMY OF EPIDEMIC ENCEPHALITIS. EUGEN FREY, Schweiz. Arch. f. Neurol. u. Psychiat. **27**:259, 1931.

Frey summarizes the results of the study of brains from persons suffering from epidemic encephalitis. Macroscopic changes were more frequent in both acute and chronic cases than is generally believed. Thromboses and areas of perivascular necrosis, furthermore, were found in some acute cases, although changes of this type in cases of epidemic encephalitis have been denied. Vascular and perivascular changes were prominent in the entire group. These findings, as well as the frequency of changes in the ependyma and subependymal tissues, in the author's opinion furnish considerable support for von Monakow's view that the vessel walls, the perivascular glia, the ependyma and the choroid plexus constitute the first line of defense against the entrance of infective agents into the central nervous system (*haemo-encéphale barrière*). Extensive cortical changes were noted in two brains. The experience of workers elsewhere relative to the activity of the glia cells, the regressive changes in the ganglion cells and the frequent involvement of the substantia nigra was confirmed. Changes in the thalamus and pallidum were less pronounced than might be inferred from a review of the literature. In a few cases, numerous foci of disease were found in the inferior olive and the dentate nucleus. Since parkinsonism has been entirely lacking in some cases in which the substantia nigra was badly damaged, and since many other parts of the brain are involved in epidemic encephalitis, Frey agrees with Bielschowsky that this and other phenomena of chronic encephalitis are attributable to a diffuse process rather than to lesions of particular centers.

DANIELS, Rochester, Minn. [ARCH. NEUROL. & PSYCHIAT.]

THE ANTERIOR LOBE OF THE HYPOPHYSIS AND GROWTH. P. VON MONAKOW, Schweiz. Arch. f. Neurol. u. Psychiat. **27**:321, 1931.

Monakow reports a case of infantilism with mental retardation in a boy, aged 7, with a mongoloid facies, who for the preceding four years had been successfully treated with a hypophyseal preparation. When first seen at the age of 6, the patient was thought to be suffering from hypothyroidism. He began to grow after the institution of thyroid medication, but the rate of growth, though normal at first, gradually became slower until his fourteenth year, when it was practically in abeyance. Treatment with thymus and various hypophyseal preparations had been ineffective. Immediately after the institution of treatment with anterior lobe substance prepared from the hypophyses of growing animals, the patient began to grow at twice the normal rate and to develop sexually, although he remained mentally retarded. Monakow expresses the belief that the

results of treatment do not warrant the conclusion that the infantilism in this case was necessarily attributable to a hypofunction of the hypophysis.

DANIELS, Rochester, Minn. [ARCH. NEUROL. & PSYCHIAT.]

POSTINFECTIVE PARALYSIS IN INFANTS. N. SASSONE, Prat. pediat. **10**:51 (Feb.) 1932.

A 16 month old baby suffered an acute attack of fever with respiratory difficulty. It was treated with diphtheria antitoxin and made a satisfactory recovery. Cultures were negative for diphtheria organisms. Four weeks later, the baby had an acute onset of fever, vomiting and diarrhea with blood-streaked stools from which enterococci and colon bacilli were isolated. No dysentery organisms could be recovered. After three weeks of intermittent, low-grade fever and intoxication, there was a sudden onset of paralysis involving the muscles of the neck and trunk but lasting only a few days. Sassone discusses the differential diagnosis at length, suggesting that the paralysis resulted from the toxic effect of the intestinal infection.

DOOLEY, Kent, Conn.

A CASE OF MONGOLIAN IDIOCY IN ONE OF FEMALE TWINS. ORESTE PENTAGNA, Actualid clin. S. Paulo **5**:38, 1931.

The author reports a case of mongolian idiocy in one of twin girls. There are signs of hypothyroidism, and he advocates thyroid therapy. From the photograph shown one might question the diagnosis of mongolian idiocy.

SANFORD, Chicago.

A MENINGEAL STATE SIMULATING TUBERCULOUS MENINGITIS. LEON VELASCO BLANCO and JUAN CARLOS BERTRAND, Arch. argent. de pediat. **2**:587 (Oct.) 1931.

The authors describe the case of an 11 year old boy who in the course of convalescence from osteomyelitis presented a clinical picture of meningeal irritation with alterations in the cerebrospinal fluid which manifested themselves by hypertension, lymphocytosis and albuminosis. The Wassermann reaction of the fluid as well as the results of the guinea-pig inoculation test for Koch's bacillus were negative. The child, however, had a positive Mantoux reaction and calcified thoracic glands.

Recovery from all symptoms occurred in a few days. The authors present an analysis and discussion of several similar cases reported in the medical literature.

SCHLUTZ, Chicago.

PARALYSIS OF THE PHRENIC NERVE IN THE CHILD. ANTONIO CARRAU and RITO ETCHELAR, Arch. de pediat. d. Uruguay **2**:14 (Jan.) 1932.

This condition occurred in a girl 6 years old, who had had contact with a person affected with active pulmonary tuberculosis.

The disorder began with a left-sided pleurisy, followed by effusion. Fluid removed from the chest showed a great many leukocytes but no organisms. Eventually the child showed massive involvement in the left lower lung, with definite signs of consolidation. Roentgenograms showed the left side of the diaphragm considerably elevated and in fixation. Paralysis of the phrenic nerve was present, and was thought to be due to an involvement of the nerve in the massive tuberculous process which had formed in this region.

SCHLUTZ, Chicago.

THREE CASES OF PROGRESSIVE NONFAMILIAL MYOPATHY. J. M. ESTAPE, F. N. REYES and P. C. BLANCH, Arch. de pediat. d. Uruguay **2**:19 (Jan.) 1932.

These cases occurred in two boys, 13 years of age, and a girl, 11 years of age. The antecedents in all three cases were healthy and well, and showed no evidence of this disorder.

In the case of the two boys, there were the classic symptoms of pseudomuscular dystrophy, with considerable hypotrophy of the muscles of the legs, the lumbar and pelvic regions and the scapulae. Both boys showed marked lordosis and considerable lividity of the skin of the extremities. There was no loss of tactile sensation or of the sphincters.

The third case had some resemblance to Friedreich's and also to Charcot-Marie's disease.

In all of the cases the disorder seemed to be moderately progressive.

SCHLUTZ, Chicago.

A CASE OF IDIOPATHIC PARALYSIS IN A CHILD FOUR YEARS OF AGE. JOSE LUIS and JULIO SANGUILY, Bol. Soc. cubana de pediat. **3**:427 (Dec.) 1931.

The condition developed subsequent to an attempt to reduce an intestinal obstruction. Diffuse tuberculosis, which was located largely in the mesenteric lymphatic glands and in the peritoneum, developed.

Medical treatment was of no avail, and an exploratory operation was performed for diagnostic purposes, in an attempt to relieve the intestinal obstruction. It was possible to relieve the condition, and the child apparently made a complete recovery.

SCHLUTZ, Chicago.

A CASE OF PROGRESSIVE LENTICULAR DEGENERATION (WILSON'S), WITH A CONSIDERATION OF SIMILAR CASES. LOUISE W. RAUH, Arch. f. Kinderh. **94**:16 (Nov. 30) 1931.

The author reports a case of progressive lenticular degeneration in a boy 11 years old. The first significant symptoms were noted at the age of 6 years when the child developed a stiff gait, particularly when fatigued, and a tremor of the hand when he wrote. He had never talked distinctly, but his speech became worse, and he began to stutter. Vomiting occurred frequently, particularly in the morning, and he drooled a great deal. When he was 10 years old he was unable to walk, and his intelligence was failing.

When seen in the clinic, the child's speech was not understandable; he had no power of concentration, and he exhibited a frequent forced laugh. There were a gross tremor of the hands and a marked tendency to pronation. If, with the arms outstretched, the head was turned to one side, the arm on that side moved in the same direction. Both legs were held stiff, the left showing a positive Babinski sign. When the left foot was elevated, there was no stiffening of the knee. In attempting to walk, he would shift from one leg to the other without being able to move forward. At the time of writing, the child was becoming gradually worse.

The author has brought together in discussion and report sixty-one other cases reported in the literature. Among the points emphasized in the discussion are the great variation in type of onset, the inevitable disturbance in gait and position of some kind, usually hypertonicity, which may lead to contracture, and the frequency with which cirrhosis of the liver is found.

The author seems to lean toward the theory that the changes in the liver are primary, leading to a disturbance in water metabolism, which in turn produces changes in the central nervous system, particularly in the lenticular nucleus and the capsule. The extent of these changes varies considerably, and the variation accounts for the different clinical manifestations.

LESLIE, Evanston, Ill.

TREATMENT OF ACUTE CHILDHOOD ENCEPHALITIS WITH LARGE AMOUNTS OF ADULT BLOOD SERUM. E. KRAMAR and G. PETRANYI, Arch. f. Kinderh. **96**:1 (March 4) 1932.

In thirty-three cases of encephalitis seen by the authors since 1925, thirteen patients were treated with large doses of serum (from 30 to 60 cc.) from the blood of adults. Two of these patients died, but both were almost *in extremis*

when the serum was given. The other eleven patients were divided into two groups: those who showed immediate improvement after the giving of the serum with a drop in temperature and clearing of the sensorium, and those in whom the improvement came on gradually. The authors realize that this is a small series of cases and that it is impossible to draw definite conclusions; nevertheless they feel convinced that this method is of great value. SCHLUTZ, Chicago.

LYMPHOCYTIC MENINGITIS OF UNKNOWN ETIOLOGY. R. GRÜN, Deutsches Arch. f. klin. Med. **172**:429 (March 21) 1932.

Grün reports twelve carefully studied cases characterized by sudden onset of headache, fever and mild meningeal signs but by few other neurologic signs. In each instance, the spinal fluid showed increased pressure and lymphocytic pleocytosis. Recovery occurred within from two to four weeks. In one case, trauma, in another, sunstroke, may have been the etiologic factor.

DOOLEY, Kent, Conn.

CATARACTS IN MONGOLIAN IDIOCY. A. ELSCHNIG, Med. Klin. **28**:217 (Feb. 12) 1932.

Cataracts of the congenital type or those developing early in infancy are rather common in mongolian idiots, but they are not typical of this condition.

In congenital cataracts operation is indicated in the first weeks, as otherwise the eyes will be blind. ZENTAY, St. Louis.

CENTRAL HYPERPYREXIA IN CHILDHOOD. M. WEICHSEL, Monatschr. f. Kinderh. **52**:37 (Feb.) 1932.

The cases of two patients who suffered hyperpyrexia for several months from no apparent cause are reported. In one child, autopsy showed pachymeningitis hemorrhagica interna. In the other, there was a hemorrhage into the suprarenals, apparently following whooping cough. The metabolism showed no abnormalities.

GERSTLEY, Chicago.

FAMILIAL LUMBOSACRAL SYRINGOMYELIA. INGEBORG WAGNER, Monatschr. f. Kinderh. **53**:137, 1932.

The author reviews the literature, and reports the case of a 15 year old girl who, since the age of 9 years, had suffered from blisters and ulcers of the toes, with no pain. There were also vasomotor disturbances in the extremities suggestive of acrodynia. The results of a careful physical examination are recorded, and the diagnosis was made by exclusion, the roentgenograms showing no spina bifida occulta.

The case is of special interest because of the consanguinity of the parents and because one of the siblings died of a similar ailment, sepsis complicating one of the ulcers. GERSTLEY, Chicago.

CHOREA MINOR. C. GRISHIN and Z. LARIN, Pediatriya **14**:493, 1930.

On the basis of the latest investigations chorea minor is to be considered an infectious disease. Analyses of the blood and cerebrospinal fluid reveal the presence of streptococci, staphylococci and other micro-organisms. These organisms, which effect inflammation of tissues, abscesses, etc., cannot, however, be held to cause chorea minor. The prominent symptoms are degenerative toxic phenomena in the nerve cells. The majority of the cases occur during the spring and summer, the season of rheumatism. Opinions exist that the condition develops during or after infectious disease. A person is predisposed to it by malnutrition, anemia, poor hygienic surroundings and heredity.

The central nervous system develops rapidly during the ages from 6 to 10 years. At this time the nervous system is most susceptible to injury. It is sufficient for a normal child to be transferred into strange surroundings or to be compelled to perform more complicated tasks for choreic movements to appear. Chorea minor appears in the majority of cases gradually.

In a great number of the cases, enlargement of the tonsils is observed; 28 per cent of the cases studied were preceded by tonsillitis.

The duration of the disease in children is approximately from forty to fifty days. It is seldom fatal, but invariably causes injury to the heart. Death is caused by severe injury to the heart.

No effective treatment other than absolute rest has been developed. Dr. Evashkewich attempted internal injections of methenamine, without any apparent satisfactory results. The authors conclude that (1) chorea minor is closely connected with rheumatism; (2) it affects the heart of the patient; (3) in the majority of cases the marks of previous chorea minor infections remain, and only in a small number of cases are no evidences of the disease left; (4) poor hygienic surroundings and weak constitution are not necessarily causes of chorea minor; (5) the hereditary factor has been established in part of the material investigated, and (6) no specific means of combating chorea minor have been developed.

YAMPOLSKY, Atlanta, Ga.

## Diseases of the Ear, Nose and Throat

INTRACRANIAL COMPLICATIONS OF OTITIC ORIGIN. I. FRIESNER and J. G. DRUSS, Arch. Otolaryng. **15**:356 (March) 1932.

Cases were studied clinically and pathologically to determine the pathologic changes and the routes taken by the extension of infection from the middle ear to intracranial structures, with the purpose of ascertaining what improvement might be made in the surgical treatment to prevent such intracranial complications. Infections of the middle ear may extend to the intracranial structures by necrosis of the bone, through fissures or dehiscences or along perforating vessels or lymphatics. The more common resulting intracranial diseases are extradural and intradural abscesses, abscesses of the brain and meningitis, local and diffuse.

Observation showed a frequency of localization, from the infections extending from the mastoid and middle ear, at the posterosuperior portion of the pyramid. An abscess of the bone may develop into an abscess of the brain in either the posterior or the middle fossa or into meningitis. The otologic surgeon must be equipped as a cranial surgeon as well, so that any evidence of extension of infection can be followed to its destination.

Nine cases are reviewed, the different phases of the subject being demonstrated.

BARNETT, Chicago.

THE HISTOPATHOLOGIC REACTIONS OF THE TRACHEOTOMIC WOUND: AN EXPERIMENTAL STUDY. LYMAN RICHARDS and FRANK GLENN, Arch. Otolaryng. **15**:389 (March) 1932.

Tracheotomy ordinarily causes obstruction grossly in the following ways: 1. Distortion of the tracheal wall from pressure of the cannula occurs, causing permanent deformity and obstruction. This distortion may involve the cartilage or the soft tissues of the mucosa or of the external structures, or there may be an involvement of all the structures. 2. Diffuse granulations form around the cannula, springing from any of the tissues involved. 3. Contractions of the scar tissue result from the granulations. The trachea tends to close as soon as the cannula is removed in many cases; hence it is often necessary to wear a cannula for many months or even years.

A series of experiments on cats was carried out to determine the histopathologic effects of tracheotomy. It was especially desirable to find out the degree of obstruction in different tracheotomy procedures in the final healing of the wounds and the type of changes that take place in the tracheal mucosa.

The following are the conclusions drawn: "1. Simple incisions in the trachea, if not infected, tend to heal with great rapidity. The defect is closed by a connective tissue growth, without any evidence of true regeneration of cartilage. The mucous membrane between heals rapidly, though with a modified form of epithelium. There is little if any tendency for encroachment on the tracheal lumen by the healing tissues in this type of wound.

"2. The presence of a tracheal cannula delays the healing of the wound and increases the amount of connective tissue formed about it. So long as there is an adequate opening in the trachea for the cannula and no pressure against the cartilaginous edges, there is very little tendency toward the formation of granulations large enough to cause any appreciable obstruction to the tracheal lumen.

"3. Infection about the cannula, occasioned primarily by too close approximation of the wound edges about the cannula, increases the tendency to connective tissue formation.

"4. With a large anterior tracheal defect there is little tendency for the superficial tissues to fall in and encroach on the lumen of the trachea.

"5. With a tracheal fistula, in the absence of a tube, the wound tends to close rapidly without any impairment of the tracheal lumen." BARNETT, Chicago.

PNEUMOCOCCIC MEMBRANOUS NASOPHARYNGITIS IN INFANTS. NOAH FOX, Arch. Otolaryng. **15**:426 (March) 1932.

The occurrence of a pseudomembranous pneumococcic infection of the mucosae of the nasopharynx and the adjacent structures is a definite entity. It varies in severity according to the extent of the mucosal involvement, the amount of ulceration and the amount of prostration present, often being fatal. Complications, such as otitis media, sinusitis, etc., are frequent and depend largely on the structures involved.

The disease is caused either by Bacillus mucosus-capsulatus, which, according to some authorities, is found in about 60 per cent of all healthy mouths, or by an organism morphologically and culturally similar to it. "Colds" seem to predispose to the disease, though otherwise previous health and living conditions may be good.

The mucosal changes are similar to those in diphtheria. There is a thick yellow tenacious membrane that leaves a bleeding surface when it is removed. It may include all of the mucous surfaces of the mouth and nasopharynx. The eyes are often involved also. Ulceration is common. The membrane is composed of pure bundles of fibrin, the interspaces being loaded with white cells and a pure growth of the encapsulated, lanceolate, gram-negative diplococci.

The onset of the disease is abrupt and severe, with an early high temperature. Toxicity develops early, with frequent toxic meningeal symptoms. Food and water are refused, and dehydration develops rapidly. The skin is dry and parched. Bleeding from the nose and mouth is frequent. The pulse is weak and rapid, but regular. Involvement of the cervical glands is common. As the membrane disintegrates, thick yellow material is deposited in the pharynx and larynx, interfering with respiration and necessitating frequent aspirations to prevent strangulation. The disease usually lasts from ten days to three weeks. Complications are pneumonia, otitis, meningitis, pansinusitis, dacryocystitis, etc. It must be differentiated from diphtheria, malignant ulcerative tonsillitis, Plaut-Vincent's infection, agranulocytic angina, and the anginas associated with the blood dyscrasias and extreme debility. The diagnosis is made definite only by the laboratory observation of the pneumococcus instead of the diphtheria bacillus.

In most cases the condition is treated as diphtheria before a diagnosis is made. Treatment should be directed toward localizing the infection in the throat and preventing dehydration. Hourly applications of a 1 per cent solution of ethylhydrocupreine by drop or spray should be given at once in the nose and throat and applied locally with dripping swabs to the other surfaces. Fluids are provided in the way that best suits the individual patient. Injections of human blood are of value. Complications are treated as they arise.

Four interesting cases are reported. BARNETT, Chicago.

LOCAL ANESTHESIA IN TONSILLECTOMY. HOMER A. TROTTER, Arch. Otolaryng. **15**:435 (March) 1932.

Local anesthesia produced by the blocking of nerves instead of the usual haphazard method of regional infiltration is possible in tonsillectomy when the anatomy of tonsillar nerves is known, and it has several advantages.

The principal deep sensory nerve supply comes from the several trunks of the glossopharyngeal with several filaments that traverse the tonsillopharyngeal bundle and occasional filaments that enter the tonsil slightly above the bundle. The arterial supply mainly follows these nerves, and together they form a kind of a peduncle, the point of attachment of which may be called the hilus of the tonsil. The other main nerve supply of the tonsillar region comes from branches of the posterior palatine nerve and is accompanied by branches of the descending palatine artery. These cross the peritonsillar space and enter the lateral surface of the tonsil above the attachment of the tonsillopharyngeus.

Actual experience has shown that if the anesthetizing solution is introduced through the lower third of the anterior pillar, with the aponeurosis being skirted and the solution finally being deposited in the midst of the tonsillopharyngeus bundle, there is produced not only nerve block but enough general infiltration in the peritonsillar space to anesthetize any nerve filaments not in the main trunks. For anesthesia, each tonsil receives 2.5 cc. of a 1 per cent solution of quinine and urea hydrochloride.

BARNETT, Chicago.

OSSEOUS CHOANAL OBSTRUCTION AND ADENOID TISSUE. C. W. GEIGER and J. H. ROTH, Arch. Otolaryng. **15**:441 (March) 1932.

A girl, 4½ years of age, had never been able to clear the left side of her nose of a glairy mucus. Excoriation and crusting were often present. The face was asymmetric and the nose long and "pinched." With the patient under general anesthesia a bony obstruction well back in the left choana was found. There was no adenoid tissue on this side, and the tonsil was the size of a large pea; on the right side the adenoid tissue was hypertrophied to obstruction and the tonsil was large and pathologic. Both tonsils and adenoids were removed.

It is not known whether complete nasal obstruction has any effect on the formation of adenoid tissue.

BARNETT, Chicago.

EPHEDRINE SULPHATE: ITS USE IN OTITIS MEDIA. ROY F. NELSON, Arch. Otolaryng. **15**:444 (March) 1932.

In acute and subacute suppurative otitis media the mucopus is aspirated as completely as possible, and a solution of ephedrine is instilled. In from ten to fifteen minutes a definite blanching and shrinking of the thick, boggy tympanic membrane is seen. This permits further evacuation of pus. The ephedrine sulphate is used alone in a 3 per cent solution or as a 3 to 5 per cent solution in a 70 per cent solution of alcohol or other antiseptic. In cases in which it seemed definite that a mastoid operation would have to be performed the condition has been cleared up by this method. The method is of especial value when the pus is thick and tenacious.

BARNETT, Chicago.

POSTANGINAL SEPSIS. ISAAC A. ABT, J. Pediat. **1**:8, (July) 1932.

A survey of the literature on septicopyemia following tonsillar and pharyngeal infections is presented, with a clinical discussion of the atria of infection from the throat, pathology, etiology, clinical course, complications, prognosis and treatment of the condition. Four cases are reported briefly, and the frequency of thrombosis of the internal jugular vein is emphasized. The treatment recommended is mostly surgical, drainage of the septic focus and ligation of the jugular vein on the affected side if there are chills and irregular fever.

LEMASTER, Evanston, Ill.

A Small Milk-Borne Outbreak of Septic Sore Throat. Robert E. Archibald and Roy F. Feemster, New England J. Med. **206**:1252 (June 16) 1932.

Twenty cases of septic sore throat were definitely traced to milk from a single cow. The rate of infection was high, 87 per cent of the persons definitely known to have used the milk raw becoming ill. There were three deaths, giving a fatality rate of 15 per cent. Two patients died of pneumonia and one of otitis media, cellulitis and septicemia. Hemolytic streptococci were found in cultures taken from the throats of fifteen of the patients and from that of the milker, and in milk from the diseased quarter of the cow's udder. No cases developed in contacts in the family not drinking the infected milk.

The usual clinical picture was that of a sudden onset with chilliness, fever and a dry, raw throat. There were also nausea, vomiting, backache and prostration. Examination of the throat showed a bright red pharynx, uvula and soft palate, no exudate being visible. In all of the cases there were more or less swelling and tenderness of the cervical glands.

Gengenbach, Denver.

A Study of the Effect of Seven Hundred and Thirty-Six Tonsillectomies and Seven Hundred and Forty-One Controls. J. D. Monroe and V. L. Volk, Rep. Am. Child Health A. **6**:15, 1929.

In this study the following conclusions were drawn from the results of 736 tonsillectomies and the observations on 741 children who refused operations: 1. Greatest relief comes from sore throats, head colds, mouth-breathing and malnutrition. 2. Complaints were relieved in the first six months in 91 per cent of the cases. 3. Operation in early childhood offers the best results. 4. Forty per cent of the mentally subnormal or retarded children were improved. 5. Coexisting conditions, except probably pulmonary tuberculosis, are not contraindications for tonsillectomy. 6. The control group showed no definite improvement in a similar period of observation. Excellent tables are furnished.

Parker, Rochester, N. Y.

Successive Bronchial Foreign Bodies. C. N. Peeler and V. K. Hart, South. M. J. **25**:729 (July) 1932.

The authors report a case of successive bronchial foreign bodies aspirated in a female child of 18 months. The bodies were aspirated in the same year, both were nonopaque and were in the right main bronchus, with obstructive emphysema on that side.

Prompt recovery followed the removal of each.

Schlutz, Chicago.

Sore Throats of Other Than Tonsillar Origin. Bedford Russell, Brit. M. J. **2**:485 (Sept. 12) 1931.

The author refers briefly to the fact that in many instances operations on the tonsils are not complete and that remnants of tonsils are left. After a review of the physiology of the nose and throat he points out that many times sore throats are due to recurrent sinusitis, with special reference to the antrum and with a secondary allusion to the ethmoid cells. A careful history, he states, in many instances will elicit the true cause of the recurrence of sore throat. He points out, by example and otherwise, that relatively young children, certainly as young as 3 years of age, have various forms of sinusitis. The sore throat in tonsillectomized patients is usually worse in the morning. Sometimes there are rashes on the skin of nose and lips, redness of one eye, pain or inflammation in one ear and an excess of secretion sticking on the hairs of one nostril. He emphasizes the fact that the discomfort is usually unilateral. Laryngeal symptoms and cough are more frequently evidence of sinusitis than they are of tonsillitis. The postnasal space should be examined carefully after the shrinkage of the nasal mucosa.

Then a trickle of mucopus may be seen coming over the posterior end of the middle turbinate, which is presumptive evidence of posterior ethmoiditis or sphenoiditis.

The treatment is then discussed and is along relatively conventional lines.

ROYSTER, University, Va.

ACUTE TONSILLITIS AND SOME OF ITS SEQUELS: EPIDEMIOLOGICAL AND BACTERIOLOGIC OBSERVATIONS. J. A. CLOVER and F. GRIFFITH, Brit. M. J. **2**:521 (Sept. 19) 1931.

Tonsillitis is considered a local manifestation of infection with hemolytic streptococci. The subsequent course of the infection is dependent on two factors, the pathogenic qualities of the infecting strain and the state of immunity of the person attacked. The site of the infecting dose is a contributory factor. It is strongly intimated in this article that, though tonsillitis and scarlatina are probably separate entities, nevertheless it is felt that the presence of the rash with the possible difference in the greater risk of nephritis makes the two one condition, both epidemiologically and bacteriologically. Infection is conveyed (1) by milk or cream, (2) by such vehicles as tableware, pencils, handkerchiefs and possibly by impure swimming-bath water and (3) by droplet infection.

In plate cultures from throat swabs taken from patients with acute tonsillitis, hemolytic streptococci are almost invariably found in profuse or even in pure culture.

There are three sequels of major importance to an attack of tonsillitis. These are scarlet fever, otitis media and acute rheumatism. The author feels definitely that scarlet fever may be referred to as the sequel to tonsillitis, quoting Trousseau's phrase: "Sore throat is an essential part of scarlet fever; it precedes the eruption."

The authors consider it as almost positive, although experimental data are lacking, that carriers are responsible for a large percentage of the outbreaks due to hemolytic streptococci. They also refer to *scarlatina sine eruption*. The bacteriologic study of scarlet fever in this article conforms more or less closely to the conventional studies already published by others. The same doubt apparently exists in the minds of the authors regarding the validity of the Dick reaction that exists in America today.

The troublesome nature and seriousness of otitis media are discussed. It is especially troublesome in large boarding schools. The experience of the authors in one boarding school showed a much higher incidence of otitis media among boys than among girls.

The troublesome question as to the relationship between the removal of tonsils and adenoids and subsequent infection of the middle ear arises in the minds of these authors, as it has arisen in the minds of most observers.

The question as to whether acute rheumatism is the sequel or complication of tonsillitis is likewise discussed, a number of authorities being quoted. It is felt that there is a definite relationship. In many instances there is the attack of tonsillitis that supplies the missing evidence in the previous history as to whether or not the patient has had rheumatism. The authors feel strongly, however, that epidemics of tonsillitis are frequently followed by severe relapses of acute rheumatism in children who have already had rheumatic treatment, and they draw the conclusion that children who have been subject to rheumatism should be protected as much as possible from any infection with the hemolytic streptococcus. Various suggestions have been made as to the care and the exercise to prevent outbreaks of acute tonsillitis.

ROYSTER, University, Va.

DIAGNOSIS AND TREATMENT OF ACUTE OTITIS MEDIA. H. B. FORSTER, Brit. M. J. **2**:645 (Oct. 10) 1931.

Acute otitis media is discussed, special stress being placed on the etiology rather than on the specific bacteriology. Heredity, according to the author, plays a part, as do also congenital defects and atrophic disease of the nose and accessory sinuses. He states finally that the lymphadenoid tissue of the upper respiratory

tract has been maligned unnecessarily. Clinical signs are given, as well as indications for incision and after-treatment. Special attention is paid by the author to the differential diagnosis of acute otitis media from other causes of acute earache.

ROYSTER, University, Va.

SUBACUTE OTITIS MEDIA. A. LOWNDES YATES, Brit. M. J. **2**:647 (Oct. 10) 1931.

Subacute otitis media is discussed in a more or less conventional manner. Nothing of special interest is added to the present knowledge.

ROYSTER, University, Va.

FOREIGN BODIES IN THE OESOPHAGUS. F. HOLT DIGGLE, Brit. M. J. **1**:277 (Feb. 13) 1932.

The author outlines his own experience with foreign bodies in the esophagus, and discusses the condition generally, especially the "unsuccessful" cases, cause of the lack of success, symptoms, diagnosis and value of roentgenology. In general, the article is along relatively conventional lines.

ROYSTER, University, Va.

CONSERVATIVE MASTOIDECTOMY FOR CHRONIC OTITIS MEDIA. L. GRAHAM BROWN, Brit. M. J. **1**:470 (March 12) 1932.

The author recommends conservative mastoidectomy for chronic suppurative otitis media, which he considers is usually indicative of mastoid involvement.

ROYSTER, University, Va.

RESULTS OF THE SO-CALLED TONSILS AND ADENOIDS OPERATION. JAMES KERR LOVE, Lancet **1**:1356 (June 25) 1932.

1. Adenoids should be removed early, and the best results are attained in the cure of mouth-breathing if the operation is followed by training of the patient to overcome the acquired habit.

2. Tonsils may often be left unless they are actually septic.

3. A discharge from the middle ear due to other causes, for example, scarlet fever and measles, is not removed by the operation on the tonsils or the post-nasal adenoids.

4. Nasal discharge is not always cured by such operations, but even in cases of apparent failure great improvement takes place.

These conclusions suggest to the author this thought: "We talk of the T and A operation: are we not the slaves of a phrase? Are we not dealing with two operations which are too often performed together? Should they not often be dissociated? The adenoid infection usually takes place earlier and the tonsils suffer first and very occasionally alone. I therefore plead for the removal of adenoids as soon as nasal obstruction occurs, leaving the tonsils unless they are evidently diseased. Where there is no history of sore throat or enlarged glands I tend to leave the tonsils." The author finds that this view results in his leaving the tonsils in from 10 to 15 per cent of these patients sent to him for operation.

LANGMANN, New York.

LATERAL SINUS THROMBOSIS WITH METASTATIC INFECTIONS OF HIP JOINT. DOUGLAS GUTHRIE, Tr. Med.-Chir. Soc., Edinburgh, 1932, p. 13; in Edinburgh M. J., February, 1932.

Several months following otitis of scarlet fever in a girl 9 years of age, there appeared headache, vomiting, fever and a rigor, without mastoid tenderness. These symptoms were due to the presence of sinus thrombosis, which was discovered by operation. Subsequent spreading of the infection required further

operative procedures. Evidently metastasis from the focus in the ear reached the hip, as arthritis then developed. Removal of the head of the femur was followed by ankylosis of the joint and, after several months, recovery.

NEFF, Kansas City, Mo.

A CASE OF FOREIGN BODY IN THE LARYNX OF A ONE YEAR OLD CHILD. A. CODINACH, Bol. Soc. cubana de pediat. **3**:371 (Oct.) 1931.

The author describes a case of a foreign body in the larynx in a 1 year old child. The patient presented a typical clinical history with the sudden onset, cyanosis, partial aphonia and fever.

The condition was not diagnosed until four months after the onset of the symptoms, i. e., at the time of the patient's admission to the hospital. The diagnosis was confirmed by roentgenologic and laryngoscopic examination. In spite of successful removal of the foreign body, bronchopneumonia developed and the patient died.

The author brings out two points of interest in this case: (1) the long duration of symptoms and (2) the unusual location of the foreign body (i. e., it was situated in the supraglottic region, firmly attached to the right vocal cord).

He mentions that in the series of Chevalier Jackson of 1,485 cases of foreign bodies removed from the upper respiratory passages there were only 5 similar cases.

SCHLUTZ, Chicago.

## Diseases of the Skin

FOLLICULITIS ULERYTHEMATOSA RETICULATA. H. G. WERTHEIMER, Arch. Dermat. & Syph. **25**:1060 (June) 1932.

The author presents a case report of a rare disease of the skin, called folliculitis ulerythematosa reticulata, occurring in a schoolgirl, aged 15 years.

The eruption appeared as symmetrically arranged lesions on the cheeks, glabella and outer portions of the eyebrows only. Clinically, the lesion was characterized by many, closely arranged, pitted atrophic areas, giving a worm-eaten appearance to the skin. Pathologically, the lesions were characterized by large, tortuous, dilated, hyperkeratotic follicles in the derma, accompanied by the usual signs of chronic inflammation.

Treatment with many methods was unsuccessful. Roentgen therapy was not used.

The disease is one of childhood. It is chronic; its etiology is unknown, and its treatment is difficult.

EKERMEYER, Iowa City.

ERYTHEMA NODOSUM: CHARACTER AND ETIOLOGY. V. H. MOON and ABRAM STRAUSS, Arch. Dermat. & Syph. **26**:78 (July) 1932.

The authors discuss the various theories concerning the etiology of erythema nodosum, including its association with tuberculosis and rheumatic fever, and the probability of its being a definite acute infectious disease.

They report experiments to give support to the supposition that this disease is caused by a specific infectious agent.

They were able to isolate and grow an organism of the genus Corynebacterium from the cutaneous lesions in three cases of erythema nodosum in human beings. These organisms were injected intravenously (and, in some cases, intramuscularly) into twelve rabbits and two guinea-pigs. Lesions histologically resembling those found in the human beings appeared in all but one of the animals. Cultures were made from the lesions of the animals, and the same organisms were found. In the control experiments, the authors were unable to find the organisms in the deep tissue of normal skin in human beings.

EKERMEYER, Iowa City.

TREATMENT OF VASCULAR NEVI BY THE INJECTION OF SCLEROSING SOLUTIONS. G. C. ANDREWS and R. J. KELLY, Arch. Dermat. & Syph. **26**:92 (July) 1932.

An effective treatment of vascular nevi is reported by the authors. They injected small amounts (not more than 2 minims [0.1 cc.]) of either quinine-ethyl carbonate (25 per cent) or a solution of sodium chloride and dextrose (50 per cent) into the lesions. The injections were made under aseptic conditions with small platinum needles. Sclerosis of the small vessels of the lesions was produced—the result desired. Twenty patients were treated effectively by this method. The authors consider the method more effective, less painful and less scarring than some other means of treatment of this condition.

EKERMEYER, Iowa City.

MALIGNANT NEUROFIBROMA OF THE SCALP; REPORT OF A CASE. ADRIEN VERBRUGGHEN and ALFRED W. ADSON, Arch. Neurol. & Psychiat. **28**:167 (July) 1932.

The authors report a malignant condition which began at the age of 8 months as a pea-sized lump behind the right ear and grew to tremendous size, with involvement of the skull and right orbit by the time the patient was 17 years of age.

BEVERLY, Chicago.

A CONDITION SIMULATING HUMAN SCLERODERMA IN RATS INJECTED WITH PARATHYROID HORMONE. HANS SELYE, J. A. M. A. **99**:108 (July 9) 1932.

In suckling rats receiving in some instances only one injection of 5 units of parathyroid extract intraperitoneally a hardening of the skin of the back shortly developed, and falling of hair over the involved area. Histologically there was marked hypertrophy of the fibrous tissue in the skin, with degeneration and deposition of amorphous calcium. This condition simulates human scleroderma and sclerodactylia. These findings tend to substantiate the idea that such cutaneous lesions are related to hyperparathyroidism. From experiments now being pursued another condition, marble bone disease (morbus Albers-Schönberg), appears to have a similar relation to parathyroid malfunction.

BONAR, Salt Lake City.

MULTIPLE NAEVI OF THE HAND. T. TWISTINGTON HIGGINS, Proc. Roy. Soc. Med. **25**:791 (April) 1932.

This case was reported in a girl aged 6 years. The left hand was the seat of multiple nevoid growths which began two years before and caused considerable deformity of the hand. One of the growths had been excised, and the section showed connective tissue with large blood spaces and many nevoid cells scattered throughout. The growths were situated deeply on the fingers.

WILLIAMSON, New Orleans.

ASSOCIATION OF EXTENSIVE HAEMANGIOMATOUS NAEVUS OF THE SKIN WITH CEREBRAL (MENINGEAL) HAEMANGIOMA. HELEN MACKAY, Proc. Roy. Soc. Med. **25**:793 (April) 1932.

A boy, aged 11 months, was first seen at 3½ months of age because of fits on the left side. He was delivered by forceps, and over the head, face and neck was a widespread nevoid port-wine stain. He was kept under observation in the hospital for six months after the onset of the fits. Twenty-four hours after a fit, the spinal fluid was found under pressure, blood stained and intimately mixed. Examination of the eyes showed the left fundus to be normal and the right optic disk to be paler and slightly larger. There was some cupping on the right, with increased tortuosity of the vessels suggestive of congenital glaucoma.

WILLIAMSON, New Orleans

ETIOLOGY OF ERYTHEMA NODOSUM. A. FIORENTINI, Clin. pediat. **14**:435 (June) 1932.

The author has studied fourteen cases of erythema nodusum in children between the ages of 3 and 14 years. The results may be summarized to show:

1. The tuberculin antireaction was clearly positive in all cases, even in dilutions of 1:100.

2. In nine cases there was a positive family history of preexistent tuberculosis.

3. One patient exhibited preexistent tuberculosis.

4. In one patient a "cold abscess" developed two and one-half months after the appearance of the erythematous lesions.

5. Examination of the hypertrophied glands of five guinea-pigs into which blood withdrawn from the brachial veins of five patients was injected, revealed acid-fast bacilli in three animals, which were killed three weeks after the inoculation of blood. The other two animals were subjected to gastric lavage on an empty stomach, and the material recovered was injected into two other guinea-pigs, both of which were subsequently shown to be tubercular.

In view of these experiences and observations, the author feels that, at least in the majority of cases, erythema nodosum should be regarded as a true tuberculous manifestation.

SIGNORELLI, New Orleans.

CAVERNOUS LYMPHANGIOMA OF THE FOREHEAD. MARTINEZ VARGUS, Med. de los niños **33**:89 (April) 1932.

A large white fluctuating mass was removed from the right frontoparietal region in an infant aged 17 months. The differentiation between lymphangioma and sarcoma is often difficult; the latter, however, is not likely to be present at birth, and it grows more rapidly. When these tumors cannot be extirpated, various irritants have been injected into them to produce sclerosis, for instance, 10 per cent solution of zinc chloride, tincture of iodine, phenol and corrosive mercuric chloride.

DWYER, Kansas City.

ALIMENTARY ALLERGY IN INFANTILE ECZEMA WITH SPECIAL REFERENCE TO EGG WHITE. A. STROBL and A. WASITZKY, Monatschr. f. Kinderh. **54**: 53, 1932.

In the serum of twenty-one exudative children, antibodies against egg white were found five times; in four instances they were in the eczema zone, i. e., obtainable with extreme dilution of the serum. Five showed antibodies against cow's milk which in three cases were in the eczema zone. The cutaneous reaction to egg white was positive more frequently than the reaction of the serum. In seven children in whom eczema developed later, the serum of one contained antibodies against white of egg and that of another against cow's milk.

Thirty patients with healed eczema under 10 years of age were tested. Three reacted to egg white (two in the eczema zone) and six to cow's milk. Cutaneous reactions to egg white were positive sixteen times. Thirteen children showed susceptibility to food, urticaria or asthma developing following specific food substances, but in only three did eczema develop.

Three adults with a history of exudative diathesis gave no positive reactions.

GERSTLEY, Chicago.

## Surgery and Orthopedics

THE DIAGNOSIS OF DISEASE OF THE HIP-JOINT WITH SPECIAL REFERENCE TO TUBERCULOSIS OF THE HIP. R. M. BURLINGAME, Am. Rev. Tuberc. **25**: 32 (Jan.) 1932.

The earliest symptom of tuberculosis of the hip in childhood is usually morning stiffness with lameness which passes off in a few hours. Later the symptoms continue throughout the day. Pain is almost invariably referred to the knee.

Night cries are frequent. Atrophy occurs early. Induration and swelling may not appear until the process is well advanced. Muscular spasm is intense and continuous, and the limb is held in flexion, abduction and external rotation. The affected leg seems longer. The chief diagnostic difficulty is differentiation from infectious arthritis, especially in the subacute stage. The history of the acute onset in infectious arthritis, the absence of demonstrable tuberculosis elsewhere in the body and negative skin tests all aid in the diagnosis. In diseases of the hip joint, beginning with pain, increased temperature and increased leukocyte count, the hip joint should be aspirated, and the fluid examined for pyogenic organisms. In coxa plana (Legg's disease), the onset is usually during the middle years of childhood (from 5 to 10 years); tuberculosis usually occurs between 3 and 5 years. In coxa plana, motion is limited chiefly in two directions, abduction and internal rotation; in tuberculosis, motion is limited in all directions. Muscular spasm is mild in coxa plana, and roentgenograms will demonstrate characteristic changes. Coxa vara presents almost the same symptoms as coxa plana, except that frequently there is external rotation. The roentgen rays demonstrate typical epiphyseal separation. Psoas abscess may be confused with tuberculosis of the hip joint, but motion is limited chiefly in extension.

SMITH, Ogden, Utah.

OSTEOMYELITIS OF THE JAWS IN NURSLINGS AND INFANTS. ABRAHAM O. WILENSKY, Ann. Surg. **95**:33 (Jan.) 1932.

Osteomyelitis of the jaws occurring in nurslings and infants has, because of its extraordinary manifestations, become separated from the general subject of osteomyelitis of the jaws and has been considered a distinct entity. This type of osteomyelitis occurs most commonly in the first few weeks of life and is characterized (1) by pathologic manifestations associated with the osteomyelitis, which are referable to the mouth, the nose, the nasopharynx and the orbit, (2) by the clinical manifestations associated with an acute infection of severe intensity, (3) by sequestration and loss of the entire jaw and of the teeth, which the disease customarily causes, (4) by the subsequent deformity associated with this loss in the fortunate patients who recover and (5) by a high mortality.

*Etiology.*—Practically all writers are agreed that osteomyelitis of the jaws must be attributed to bacterial infection. In infants pneumococci and streptococci are the commonest organisms, while in older children staphylococci are. The available sources of the infecting organism are (1) the vaginal canal of the mother, (2) the fingers of the accoucheur or nurse, (3) the nipples and breasts of the mother and (4) the fingers or apparatus used in cleansing the baby's mouth.

*Clinical Course.*—In 82.5 per cent of the cases reported in the literature, the first two months of life were involved. The disease usually affects healthy infants. The prodromal symptoms may be insidious or abrupt. Then the swelling appears. It may begin in the cheek or in the infra-orbital region, and almost always is accompanied by edema of the orbit. Most of the children are really sick. The temperature is irregular; convulsions are frequent, and anorexia common. Often there is a purulent discharge from the nares. Usually as a final stage a large abscess cavity forms, which harbors the entire necrotic jaw.

*Treatment.*—In severe toxic cases treatment may be only palliative; in mild cases, (1) first careful cleansing of the mouth and possible poulticing are indicated; then (2) as soon as fluctuation occurs, adequate incisions, performed as much as possible from the interior of the mouth and through the nasal cavities, are indicated.

BANTIN, Omaha.

CONGENITAL HYPERTROPHIC PYLORIC STENOSIS IN INFANCY. E. J. DONOVAN, Ann. Surg. **95**:174 (Feb.) 1932.

The author reports his experiences in a study of 119 consecutive cases of congenital hypertrophic pyloric stenosis in infancy. The symptoms recorded are

those usually associated with the condition. The onset occurred at any time from birth to 10 weeks of age. Vomiting was always the first symptom. It was often projectile but never contained bile. Malnutrition, dehydration and rapid loss in weight were additional symptoms.

The preoperative preparation of the patient is greatly stressed, and is regarded as the most important factor in lowering the operative mortality. The operation is no longer considered an emergency measure. If the baby is in a bad condition, it is given one or two preoperative transfusions, using 20 cc. of whole blood for each kilogram of body weight. All patients receive from one to four hypodermoclyses of 100 cc. of 3 per cent dextrose solution before operation. In order to maintain the body heat during operation, a hot water bottle is placed under the child on the operating table. Just before the abdominal incision is made, the stomach is emptied by passing a soft catheter, size 18 F. The operation done is the Fredet-Rammstedt submucous pyloroplasty. Ether by open cone was used in all but three operations, these being performed with procaine hydrochloride because of respiratory infection.

From the operating room the child is taken to a room with a constant temperature, used exclusively for these cases. The head of the bed is lowered until the child recovers from the anesthetic, to prevent aspiration of mucus. Two hours after operation 15 cc. of water is given by mouth, and four hours after this the first feeding of 4 cc. of breast milk and 4 cc. of barley water is given. The breast milk and barley water are increased from 5 to 10 cc. with each three-hour feeding until the child is taking 30 cc. at the end of forty-eight hours. The breast milk is then increased from 5 to 10 cc. daily until the requirements are met. One or two clyses of 3 per cent dextrose solution are given each day for the first three days. All feedings for the first five days are given with a medicine dropper. Breast-fed infants are allowed to nurse once on the fifth day, twice on the sixth day and so on until they are completely breast fed.

The author closes with a detailed report of the 7 deaths in the series of 119 cases.

BANTIN, Omaha.

PREOPERATIVE AND POSTOPERATIVE CARE OF CONGENITAL CLEFTS OF THE LIP AND PALATE. EDWARD A. KITLOWSKI, Ann. Surg. **95**:659 (May) 1932.

Since the age of the patient and the location of the field of operation materially increase the operative risk, the preoperative and postoperative care is important. While there is still some difference of opinion as to the best time at which to correct the defects, Kitlowski believes that the cleft lip should be repaired as soon after birth as possible, depending on the nutrition and vitality of the infant. The closure of the lip can be delayed until some time before the end of the third month if necessary, but the most favorable time is within the first six weeks. The best time for the repair of the cleft palate is between the ages of 18 months and 2 years.

The preoperative care for the infant with a cleft lip is as follows: If the infant is in poor condition, it should be admitted to the hospital as soon after birth as possible and at once placed under the care of a pediatrician for supervision of the feeding. When it has reached a normal birth weight, usually operation can be safely risked. The mouth is carefully cleansed with boric solution after each feeding. In addition to milk, orange juice with cane sugar is given twice daily, and sodium bicarbonate three times daily to prevent acidosis after operation. The Wassermann reaction, hemoglobin content, bleeding time and clotting time of the blood are determined. If the hemoglobin content is below 70 per cent or if jaundice is present, operation is delayed. The patient is given daily exposures under the ultraviolet ray lamp, and transfusions of whole blood are given if the condition is very poor. Two drops of 20 per cent mild silver protein are put into each nostril three times daily while the patient is waiting for operation. The presence of an enlarged thymus is not given any special consideration. This preparation takes from a few days to several weeks.

The preoperative care for the patient with a cleft palate is slightly different because the patient is older. The parents are questioned about the diet and the gain in weight. The patient is given orange juice with sugar and sodium bicarbonate, and mild silver protein is used in the nose. The blood and urine are again checked. The past history as regards respiratory infections is investigated (there should be an interval of three months between the last disease and operation). If the tonsils and adenoids are infected, they should be removed and the operation for cleft palate delayed for at least three months. All decayed teeth should be taken care of.

Food is given to both the patient to be operated on for cleft lip and the one to be operated on for cleft palate until eight hours before operation, and water is given until they are sent to the operating room. No drugs or sedatives are given preoperatively to children under 2 years. The anesthetic used is ether, given by the drop method.

After operation, the patients are placed in warm beds, on their abdomens, with heads turned to one side so that mucus can run out. A nurse is in constant attendance until consciousness returns. Codeine sulphate is given by hypodermic injection to patients with cleft palate and camphorated tincture of opium to those with cleft lip. Those with cleft palate are given nothing by mouth for twenty-four hours, but the patients with cleft lip are given sterile water as soon as they can swallow. All are given proctoclysis every four hours until they take fluids by mouth. The arms and legs are restrained. After the tenth day, the patients operated on for cleft palate are given a very soft diet of cooked cereals, soft boiled eggs, custards, etc.

BANTIN, Omaha.

EWING'S SARCOMA. CARROLL BROWN, J. South Carolina M. A. **28**:33 (Feb.) 1932.

A case of Ewing's sarcoma of the left tibia and fibula is reported in a boy 14 years of age. His previous history was good, except that he had had an infectious mononucleosis in August, 1930, from which he recovered completely. In March, 1931, he began to complain of pain in the left leg, and roentgen examination revealed a tumor mass in the bone. Biopsy of an inguinal gland was negative for malignant change. The condition responded to irradation, and on Nov. 23, 1931, the patient was still improving. The rapid response to treatment founds the belief that this is a case of Ewing's sarcoma.

WESTON, Columbia, S. C.

THE TREATMENT OF EARLY CASES OF KNOCK KNEE AND BOW LEG IN CHILDREN. EDGAR CYRIAX, Brit. J. Child. Dis. **29**:35 (Jan.-March) 1932.

Cyriax believes that a number of cases of these deformities are primarily due to a loss of equilibrium between certain groups of muscles. In knock-knee, the chief disturbance of equilibrium results from the internal rotators not being strong enough as compared with the external rotators of the hip. Less frequently, the abductors are too weak in comparison with the adductors. These differences are in all probability due to retarded development in the weaker groups, and not to excessive development in the stronger antagonists.

The treatment of early knock-knee is reeducation, i. e., active effort on the part of the patient. The so-called resisted exercises applied according to the Swedish system of Ling are the ones advocated. Massage in the form of stimulatory pétrissage and limited to the weakened muscles is also indicated.

In bow-leg, it is generally the adductors of the thighs that are too weak as compared with the abductors. The treatment of the adductors is carried on by means of resisted exercises plus stimulating pétrissage of the weak muscles.

LANGMANN, New York.

ACCIDENTS TO THE NERVES FOLLOWING REDUCTION OF CONGENITAL DISLOCATION OF THE HIPS. PIERRE CORRET, Rev. d'orthop. **19**:5 (Jan.) 1932.

Accidents to the nerves following closed reduction of congenital dislocation of the hip are rare. Froelich gives an incidence of 10 in 2,600 cases. Lorenz states that he has seen paralysis of the sciatic nerve 23 times in 755 cases. Taylor has had 9 cases of paralysis of the crural nerve in 50 dislocations. The accident seems most liable to follow reduction in the cases in which the child reaches the age of from 5 to 9 years before reduction is attempted, and in which the head of the femur lies 5 cm. or more above the fossa.

The symptoms may develop immediately, may be delayed for hours, or may appear after twenty-four hours have elapsed. There is flexion of the toes, loss of the plantar reflex, loss of motion of the leg and flail foot. Incontinence of urine may occur and may persist for fourteen days or more. The paralysis may disappear after twenty-four hours, only to return. Temperature of the leg is slightly elevated; some edema is present, and the skin is red and moist. Paralysis of the crural nerve remains for approximately four months; that of the sciatic nerve for six months. The sciatic popliteal externus requires the longest time to cure.

Prophylaxis is the best treatment; slow, continued traction to pull the head of the femur down to the acetabulum must first be used in all cases in which the head lies 5 cm. or more above the brim. If paralysis appears, lessening of the abduction or removal of a window in the plaster cast may be performed to release the pressure on the nerve and permit electrization of the muscles of the leg and foot. Since the tendon of the pyramidalis is usually the principal agent in the compression, Gocht suggests a tenotomy of its tendon.

Cerebral accidents following reduction of congenital dislocation of the hip by the closed method are rarer still than the foregoing. Race seems to play a part in their occurrence, Jewish and Oriental persons being most likely to show such injuries. These accidents fall into two groups: those which follow a cerebral embolism, and those in which there does not seem to be any known cause.

The symptomatology of the second group will have its origin in the reflex system; there will be headache, restlessness, slight elevation of temperature and mild convulsions, which appear several days later. Some authors consider fatty embolism as the cause of the symptoms; here apathy, deep sleep and almost coma occur, followed by death.

The pupillary reflexes are variable, and respirations of the Cheyne-Stokes type.

In spite of all the explanations, fat embolism shows many obscurities in its presentation. However, it is quite possible that thrombi are produced either by the manipulation or as a result of the excessive hematoma about the joint. These may be the source of the emboli. Laubry has shown that defects in the interauricular septum occur in about 15 per cent of infants. This percentage will be present, or even increased, in children with other deformities, such as congenital dislocations.

Treatment consists of prophylactic doses of bromide and immediate removal of the plaster cast, with relaxation in the position of the leg if convulsions occur. Chloral, an ice cap applied to the head and cardiac tonics are usually sufficient as symptomatic treatment. In every case a complete examination of the heart, urine and nervous system should be made previous to any attempt at reduction.

RYAN, Vancouver, B. C.

FRACTURE OF THE NECK OF THE FEMUR IN A CHILD. SUBSEQUENT COXA VARA FRACTURE DEFORMITY. ROGER PETRIGNANI, Rev. d'orthop. **19**:41 (Jan.) 1932.

Fractures of the neck of the femur in children and in adolescents are exceptional. The case reported was seen two years ago and has been followed throughout that time. The fracture was reduced and held in place by plaster spica of the Whitman type. At the present time, coxa vara is present, and this raises the question of whether or not the coxa vara was caused by the fracture. Fractures of

the neck of the femur in children are, as has been stated, rare. The author believes that 90 per cent of the cases published as fracture have, in fact, been wrongly diagnosed (rachitic coxa vara, with secondary traumatism, would, he says, be more correct). Rachitic coxa vara, discovered after a trauma, is very likely to lead to a mistaken diagnosis. Here the rachitic deformity is the major lesion and the fracture secondary.

The orthopedic treatment of these fractures demands an exact reduction followed by prolonged immobilization in a plaster cast, and lastly, care and extreme precaution in finally permitting free weight bearing without support.

RYAN, Vancouver, B. C.

TREATMENT OF BURNS. G. MECCA, Prat. pediat. **10**:61 (Feb.) 1932.

This is an argument for conservative treatment of burns in infants. The author applies a bland, antiseptic ointment and covers the burn with a ventilated box rather than with gauze dressings.

DOOLEY, Kent, Conn.

OSTEOMYELITIS OF THE SUPERIOR MAXILLA IN BABIES. D. BOSSE, Arch. f. Ophth. **126**:465, 1931.

The ophthalmologist should know about this disease, of which the author observed three cases. The babies are usually brought to the ophthalmologist with the symptoms of swelling of one or both lids, sometimes accompanied by signs of an orbital phlegmon. One might first think of a phlegmon starting out from the tear sac which possibility is usually ruled out by the absence of pus in the sac. One might also think of thrombosis of the cavernous sinus. In the latter condition both eyes are affected, and cerebral symptoms are present. The main sign of osteomyelitis of the superior maxilla is a fluctuating abscess in one lid with swelling of the entire maxilla and (usually) pus in the nose. The treatment of these babies should be in the hands of the surgeon or oral surgeon. The abscesses have to be opened; incisions of the lids should be avoided if possible, because they always lead to ectropion and require plastic operations later. Deformities of the superior maxilla are always the result of the osteomyelitis. The parents of the patient should be told that these deformities will become manifest at the age of 6 or later, and that treatment by the oral surgeon will be necessary.

KRONFELD, Chicago. [ARCH. OPHTH.]

THE PROBLEM OF THE UNDESCENDED TESTIS. E. HEINICKE, Deutsche Ztschr. f. Chir. **235**:344 (Feb. 25) 1932.

The failure to obtain completely satisfactory results in operation for undescended testicle is greater than is generally suspected. The cause of failure of the testis to descend is not as yet understood. The author listed the theories as follows: primary failure of development of the scrotal sac; abnormal narrowness of the inguinal canal; abnormal smallness of the external inguinal ring; overdevelopment of the aponeurosis of the internal abdominal oblique muscle; abnormal shortness of the ductus deferens; abnormal shortness of the vessels of the testis; a primary lesion of the internal spermatic artery leading to atrophy and associated failure of descent of the testis; failure of development or false insertion of the gubernaculum; abnormal shortness of the mesorchium; intra-uterine injury to the perineal region such as might be caused by pressure of the infant's heel; intraperitoneal scars, possibly secondary to fetal peritonitis or to trauma due to pressure or friction in the peritoneal cavity. Many consider the condition as an atavistic evolutionary tendency. No theory is completely satisfactory. In Heinicke's series, a hereditary factor could not be established. Two brothers were observed who had bilateral undescended testes, but the father was normal. Occasionally associated anomalies of development were observed, such as hydrocephalus, tower skull, idiocy and others. According to the author, there seems to be no failure of development of the interstitial cells in undescended testes. Also, it is not absolutely true that

failure of descent always means failure of sperm formation, though this is a rather general opinion. The series was not studied from this point of view.

As a rule, the younger a patient is when operated on, the less primary atrophy of the testis will be found. In patients up to 7 years of age in Heinicke's series there was no difference in size between the normal and the undescended testis. In patients over 7 years of age there was a demonstrable difference in about 58 per cent of the cases, the percentage showing differences being about the same before and after puberty. The author was able to demonstrate what might be termed compensatory hypertrophy of the normal testis in only one case. As a rule, the transplanted testicle, if not markedly atrophied, grows well after operation. The type of operation employed must vary with the individual case, but the principle underlying all operations is to bring the testicle into the scrotum under the least possible tension. The author stated that the tendency of the undescended testis to undergo malignant degeneration has been overemphasized and does not justify too radical an operative procedure, such as castration. In the Eiselberg Clinic it is the opinion that it is better to bring the undescended testis into the abdomen, where the blood supply is undisturbed, than into the scrotum under tension. In either case, the prognosis is poor as regards spermatogenesis, the theory being that in the abdomen the higher temperature inhibits sperm formation.

Of Heinicke's thirty patients, seven were between 1½ and 6 years, nine between 8 and 12 years, three between 14 and 16 years, ten between 19 and 25 years, and one was operated on at 64 years because of the association of the undescended testis with a huge hernia. In four, the cryptorchidism was bilateral; in seventeen the undescended testis was on the right side, and in nine, on the left side. In the majority of published reports the tendency of the undescended testis to be on the right side is noted, and this predisposition is probably associated with the natural tendency of the right testis to descend later than the left. In 83 per cent of the cases there was an associated hernia or an open vaginal process. In no case did a hernia occur or recur after operation. Satisfactory postoperative results were obtained in about 50 per cent of the cases. In about 18 per cent of the cases there was postoperative atrophy of the testis about the usual percentage reported by other surgeons. Downward massage of the testis, administration of hormone (names of preparations and other details concerning this were not mentioned) and possibly diathermy were recommended as postoperative measures.

In conclusion, Heinicke states that cryptorchidism is to be regarded as a disturbance of development and the expression of a general tendency toward failure of development, which may be expressed generally or limited only to the genitourinary tract. Atrophy of the undescended testis is probably secondary to a certain primary tendency to hypoplasia. It is recommended that the operation be carried out in early childhood, presumably before the age of 7 years.

GLASER, Rochester, N. Y.

THE CONSERVATIVE TREATMENT OF EMPYEMA. K. LEWKOWICZ, Monatschr. f. Kinderh. **52**:151 (Feb.) 1932.

Case reports and conclusions favor the closed treatment of empyema. The intrapleural injections of ethylhydrocupreine were successful in sterilizing the pleural fluid, but did not result in absorption of the exudate.

The article is interesting on account of the excellent and original clinical charts.

GERSTLEY, Chicago.

## Miscellaneous

IMMUNITY IN GENERAL AND IN CHILDREN IN PARTICULAR. DOMENICO VACCARI, Clin. pediat. **14**:479 (June) 1932.

After an extensive and detailed review of the subject of immunity in all its phases, the author reports the results of his experiments on a series of patients and on a larger series of guinea-pigs. His object was to determine whether the hypodermic injection of very small doses of diphtheritic toxin would result in the establishment of an active immunity.

He found that the inoculation of even so small a dose as from one fiftieth to one tenth of the minimum lethal dose of diphtheritic toxin in a guinea-pig stimulated a determined production of antitoxin. This reaction was repeatedly checked with Schick tests. It was found that repetition of the inoculation at intervals of from nine to twelve days until four doses were given established an immunity of such a degree as to permit the animals to withstand the inoculation of diphtheritic toxin in amounts varying from two to three times the lethal dose without the development of symptoms.

All these experiments were checked with control tests in animals not so inoculated, which succumbed to diphtheria in each case.

SIGNORELLI, New Orleans.

EDUCATIONAL AND SOCIAL FUNCTIONS OF THE PLAYGROUND. ERNESTO NELSON, Bol. Inst. internac. am. de protec. a la infancia **6**:6 (July) 1932.

The author states that psychology teaches that the function of our physical life is to modify our motive reactions so as to adapt them to environment, and thus obtain life, pleasure and efficiency. The school does not give due attention to its duty of organizing the life of the child and of provoking, controlling and improving its bodily motive coordination. It would seem that sight had been lost of the true objective of the school, which is not science but the building up of strong, well balanced men and women, enabled to face the battle of life.

The public playground has appeared and has entered into possession of an abandoned soil, its value consisting not only in providing open-air play, but in having mastered the educational and social values of play. Play is a factor of the highest quality in physical education. It is the greatest producer of health, as well as an excellent means of moral exercise and a factor of social economy in child guidance.

The equipment of playgrounds differs according to the children's age and the end sought for in each individual or social case. Gulick says on this theme: "The sand-pile for the toddler, the playground for the child, the athletic group for the youngster, traditional dances and ceremonies for the adolescent, healthful opportunities of social intercourse for the adult: such are the social conditions without which democracy cannot subsist, because on them rests the development of self-government, which also leads to the understanding of the needs of others."

The care of animals and plants and work in factories offer other opportunities for the useful employment of leisure hours, which is an efficient means of preventing juvenile delinquency.

The author draws attention to the fact that in South America, Uruguay is the country that has had the honor of first carrying into effect these leading principles, with wonderfully organized playgrounds. AUTHOR'S SUMMARY.

PHYSICAL EDUCATION IN BOLIVIA. SATURNINO RODRIGO, Bol. Inst. internac. am. de protec. a la infancia **6**:35 (July) 1932.

The first serious step toward the organization of physical education in Bolivia was taken in 1909, but the teaching was not confided to special teachers until 1914, when the General Direction of Physical Education was established. This official agency centralizes all physical education activities, framing the school programs and controlling the different aspects of all such activities in and outside the school and in public and private institutions. The different sporting and athletic organizations must register in the General Direction, which provides them with the necessary credentials to participate in the contests.

Physical education is thus organized in the schools: Thulin's principles in the kindergarten and the first and second grades of primary schools; Ling's Swedish gymnastics from the third to sixth grades of primary and from the first to third grades of secondary schools; maintaining gymnastics in the fourth grade, and Hébert's natural gymnastics in the fifth and sixth grades of secondary schools.

The teachers are trained in the Higher Institute of Physical Education, where they follow an extensive three-year course; to enter the Institute it is necessary to have a bachelor's or normal teacher's degree and to be a native or naturalized citizen of Bolivia.

Some public and private schools have established scout brigades, but the organization has not flourished, owing to economic factors.

Gymnastics is compulsory, with the following weekly program in every school: three hours for exercises; three hours for games; one afternoon at least for an excursion, and sports combined with games and excursions.

There are parks in the departmental capital cities, where the pupils go with their physical teachers; in La Paz there are four special playgrounds for children.

Each of the five chief cities is provided with a stadium; the La Paz Stadium when finished will seat 50,000.

There are athletic associations in all the departments, with a central organization in La Paz called the National Athletic Federation; the School Sporting Association is being organized.

Sports were introduced into the schools in 1914, when the first teachers of physical education finished their training course at the Sucre Normal School.

AUTHOR'S SUMMARY.

INTERNATIONAL ASSOCIATION FOR PREVENTIVE PEDIATRICS. MARTINEZ VARGAS, Med. de los niños **32**:289 (Oct.) 1931.

This paper concludes a discussion of preventive measures in pediatrics during an assembly at The Hague in September, 1931. Immunization against scarlet fever with the toxin of Dick is described, as well as deaths occurring in the first year of life and the prevention of tuberculosis, syphilis and smallpox.

DWYER, Kansas City, Mo.

ADVICE TO MOTHERS. MARTINEZ VARGAS, Med. de los niños **32**:321 (Nov.) 1931.

This article is an address broadcast by radio which deals principally with the high mortality in infancy, the importance of breast milk, weaning from the breast and artificial feeding in early life. DWYER, Kansas City, Mo.

THE GOLDEN JUBILEE OF DR. MARTINEZ VARGAS. Med. de los niños **32**:354 (Dec.) 1931.

This number is devoted to the golden jubilee of Dr. Martinez Vargas' fifty years in medicine. The nestor of pediatrics in Spain celebrated his seventieth birthday on Oct. 17, 1931. After graduation in 1881 from the University of Saragossa, he studied in New York with Jacobi in 1884. His contributions to medical literature have been numerous and are listed in serial order in this number. Numerous testimonials from his friends testify to his scholarly attainments as a publicist and an investigator. He has been the editor of *Medicina de los niños* since it was founded in 1900. DWYER, Kansas City, Mo.

THE USE OF DYES IN THE TREATMENT OF INFANTS. ANTONIO LLAURADÓ TOMÁS, Med. de los niños **33**:1 (Jan.) 1932.

The author discusses the bactericidal action of various strengths of mercurochrome-220 soluble against the staphylococcus, streptococcus, gonococcus and other organisms *in vitro*. This agent was also used on guinea-pigs. One per cent mercurochrome solution was given intravenously in the following amounts: 0.15 cc., 0.35 cc., 1 cc., 2 cc. and 8 cc. Autopsies were performed to ascertain the effect of the dye on the organs.

It was found that very small doses, ineffectual from the therapeutic point of view, produce easily recognizable lesions in the kidney. The lesion is degeneration of cells of the convoluted tubules. Mercurochrome is eliminated by way of the kidney tubule.

The dose is from 1 to 8 mg. per kilogram of body weight in a 1 per cent solution when used intravenously and in a 5 per cent solution for disinfection of the skin. Mercurochrome is precipitated by the alkaline salts, weak acid, urea and quinine hydrochloride.

DWYER, Kansas City, Mo.

INFANTILE MORBIDITY AND MORTALITY IN THE YEARS 1926 TO 1930. T. TAMBURRI, Prat. pediat. **10**:147 (April) 1932.

This article is a detailed statistical study compiled from the case histories of 5,650 patients in the Hospital of St. Martin, and presented at the Genoa Regional Congress of Pediatrics in January, 1932. The incidence of all types of disease was greater in boys than in girls. The mortality also was greater among boys except in infectious diseases in which the mortality among girls was higher save in poliomyelitis. At the age of 10 years, the morbidity index was the same in both sexes, but in the ensuing two years of life there was a relative increase among girls, doubtless the result of the earlier puberty in the female sex. The author interprets his study as indicating the physical superiority of the female.

DOOLEY, Kent, Conn.

HEREDITY AND EDUCATION. ENRIQUE SUÑER ORDONEZ, Pediatria españ. **21**:481 (June) 1932.

As regards heredity and education, patients can be divided into three kinds: (*a*) normal, (*b*) neurotic and (*c*) degenerate. The first two groups are modifiable; the last is not.

In normal and neurotic patients (in the sense of Oppenheim), the initial education is of prime importance. In the formation of will, character and moral personality, the contradictory expressions of impulses or prejudicial inhibitions play a fundamental rôle. Uninterrupted education is the pedagogic ideal. The system must permit individualization and must adapt itself to the peculiarities of every case.

The transmission of normal or abnormal physical characteristics can be explained better on a dynamic than on an anatomic hypothesis. All hypotheses formulated—the anatomic, dynamic, physical and chemical—cannot explain the higher spiritual functions such as the evolution of creation, the indestructible firmness of character and the moral fortitude, for example, of saints and heroes, which is influenced in no degree by adverse suggestion. The author believes that only independence of the spirit or soul from matter can explain these phenomena. The biologic mechanism in these cases is the instrument of the spirit or soul.

SCHLUTZ, Chicago.

DISTRIBUTION OF SIGAND'S CONSTITUTIONAL TYPES AMONG INFANTS IN EAST PRUSSIA. GERHARD RETFELD, Arch. f. Kinderh. **97**:11 (July 22) 1932.

Two hundred and forty infants in East Prussia were examined and classified according to Sigand's differentiation of four constitutional types: cerebral, respiratory, muscular and digestive. The large number of infants found to be of the muscular type is explained by the fact that their parents were mostly of the laboring and farming class. The author believes that in the future increase in the knowledge of constitutional types will prove of value to teachers and doctors.

LEMASTER, Evanston, Ill.

WHAT HAS SIGMUND FREUD DONE FOR PEDIATRICS? JOSEF F. KRIEDJUNG, Kinderärztl. Praxis **2**:289 (July) 1931.

Freud has taught pediatricians the necessity of studying the psychology of the child and of modifying his conception of the family idyl. Side by side with love

there may frequently be jealousy, envy, competition and even open hate, which may have a profound effect on the building of character. Of especial importance is the relationship between mothers and sons and fathers and daughters, the so-called Oedipus and Electra complexes. In states of fear, anorexia, and the like, it is of great importance to develop the history along the lines of these family conflicts. Freud has taught us to understand many conditions due to faulty environment: the peculiarities of the only child, the favorite child, and the unloved, fought-over or dethroned child; the conflicts between sisters, and the fate of the middle child. Friedjung gives a list of common symptoms which may result from such emotional conflicts: anorexia, habitual vomiting, obstipation, diarrhea, umbilical colic, enuresis, pollakiuria, stuttering, mutism, nervous cough, pseudocroup, bronchial asthma, blepharospasm, partial and total amblyopia, hallucinations of sight and hearing, hyperesthesia, paresthesia and anesthesia of the skin and of taste and smell. These symptoms must not be treated as separate conditions but must be regarded as one part of the picture of general neurosis or hysteria. Freud does not regard masturbation as a neurotic symptom but rather as physiologic and harmless. The value of a change of environment as a therapeutic measure is recognized, but its effect is of little permanent value, unless there is improvement in the original environment to which the child must ultimately return. Such a change in the family environment can only be brought about by psychoanalytic methods, even though actual psychoanalysis is necessary in comparatively few cases.

Freud has taught pediatricians to regard nursery schools and kindergartens as something more than sources of infection. For a long time Friedjung has advocated a law demanding enforced attendance at nursery schools and kindergartens; recently the Vienna Pediatric Society has endorsed this stand.

Freud's work has immeasurably increased the importance of pediatricians, but not all of them have responded to the opening up of this new sphere of influence.

HUENEKENS, Minneapolis.

THE SIGNIFICANCE OF THE INVESTIGATION OF ALLERGY FOR THE PEDIATRICIAN. ALBERT UFFENHEIMER, Kinderärztl. Praxis **2**:545 (Dec.) 1931.

The author includes under allergic conditions, bronchial asthma, eczema, conjunctivitis, rhinitis, bronchitis, tonsillitis and Quincke's edema. Eosinophilia is accorded especial significance, so much so that in each case a graph is made of the counts for eosinophilia. The count is low during the acute attacks of the allergic condition and rises during the subacute or chronic stages, returning to normal when a more or less permanent cure has been effected.

For both diagnostic and therapeutic purposes, mixed allergens with liquid are employed; that is, meats are combined in a single mixed allergen, and vegetables in another, as are fish, bacteria and pollens. For diagnosis, the liquid allergen is first applied cutaneously; if there is no reaction, on the following day it is injected intracutaneously in a 1:1,000 dilution; if still negative, this is followed on the next day by a 1:100 dilution, and on the fourth day by a 1:10 dilution. When a positive diagnosis is made, the allergen is injected subcutaneously for therapeutic purposes, the initial dose depending on the severity of the diagnostic reaction. In some cases the initial therapeutic dose is given in a dilution as low as 1:5,000,000 and gradually worked up to a 1:5 dilution. Great caution must be exercised in increasing the dosage, in order not to cause a severe reaction. A series of interesting case histories is presented.

HUENEKENS, Minneapolis.

IODINE POISONING FOLLOWING THE USE OF IOPAX. D. TSAMPLAKOS, Med. Klin. **27**:1353 (Sept. 11) 1931.

Two women were given iopax for the purpose of pyelography. Immediately after the intravenous injection, an urticarial eruption appeared on the extremities and the face, followed by edema of the eyelids, lips and ears. Visual disturbances

and dizziness were noted. The reason seems to be sensitivity to iodine. The author advises that patients be tested for this possibility before being given intravenous injections of iopax.

ZENTAY, St. Louis.

EXAMINATION OF AUTHORITY AS A FORM OF SOCIAL INFLUENCE. RUTH KLEIN, Ztschr. f. Kinderforsch. **39**:249 (Feb. 8) 1932.

The author, who is in the Psychological Institute of Buehler in Vienna, presents a minute examination of authority in the development of the child. She first examines the subject from the standpoint of its definition and shows that the different psychologic and pedagogic schools vary in their interpretation of the term. She points out that there is a very strong movement at present in the modern school against the use of authority—under which is understood a conscious control and position of superiority held by the adult and impressed on the scholar. She also points out that the individual-psychologist regards authority as one of the primary causes of the inferiority complex. The psycho-analyst, on the other hand, considers the position of authority exerted by the father as the source of neuroses.

The author then passes on to a practical experimental examination of situations artificially produced among children of different ages, and divides the general subject of authority into two objectively tangible complexes: the adult's influence and the child's recognition of such influence. She regards these two as the chief characteristics of authority. She finds that even the young child reacts to commands and prohibitions, first with an entirely reflex action, later with a reaction to suggestion and finally with an indivdual type of reaction, and that these children carry out the commands of the adult despite internal inhibitions which show themselves in expressions of temperament. She discovers that at a very early age there is a spontaneous movement of the child toward the adult in the attempt to obtain sympathy or understanding and that later, as the child grows older, this appeal to the adult directs itself toward some specific request for aid or protection. In other words, the reader leaves the article with a feeling that the author has shown that authority is by no means a foreign impression on the child's character but that it satisfies the child's spontaneous demand.

REICHLE, Cleveland.

THE SEXUAL CONSTITUTION. THEODOR HELLER, Ztschr. f. Kinderforsch. **40**:72 (April 22) 1932.

Heller describes cases as belonging to a sexual constitution which shows premature development of sexual feelings and instincts in such a fashion as to disturb the development of character and temperament. This sexuality is not periodic but governs the child's entire life and adapts itself to the particular circumstances, so that not infrequently perversities arise. Heller does not believe that the cause of this condition is necessarily found in the child's environment. He regards the prognosis as grave, since this condition is combined with severe defects of character. A frequent result is a neurosis or hysteria, which represents an attempt of the individual to find a release in his illness. There seem to be more females in this group than males. Heller considers it probable that many of the cases of sexuality in children described by psycho-analysts belong to this group. He does not agree with Freud that prominent sexual inclinations are frequent among normal children.

REICHLE, Cleveland.

INFLUENCE OF FATHER'S UNEMPLOYMENT ON SCHOOL REPORTS OF CHILDREN. A. BUSEMANN and G. HARDERS, Ztschr. f. Kinderforsch. **40**:89 (April 22) 1932.

As was to be expected, the authors find that the unemployment of the father has a serious effect on the school reports of the children. Apparently, the girls suffer more than the boys, and the younger children more than the older ones.

REICHLE, Cleveland.

CAUSES AND TYPES OF ASOCIAL CHARACTER SEEN IN FORMER STUDENTS OF SPECIAL CLASSES. CLEMENS WEMMER, Ztschr. f. Kinderforsch. **40**:105 (June 27) 1932.

The author has studied the life of students who have been released from special problem classes. He comes to the conclusion that the inherited character of these persons was rarely of itself responsible for the development of an asocial life. External factors were almost always to be found which acted as an injurious influence on the weakened resistance of the person. It is therefore not correct to assume that in these especially predisposed children criminal or asocial characteristics must necessarily develop. Careful observation and the removal from a poor environment will often prevent their deterioration. However, after an asocial tendency has once developed, it is difficult to cure. Hence, here too prevention is much better than therapy.

REICHLE, Cleveland.

INSTRUCTION IN SEXUAL HYGIENE. WERNER GOTTSTEIN, Ztschr. f. Kinderforsch. **40**:219 (June 27) 1932.

This article calls attention to certain practical details of sex education which are usually neglected in theory and practice. Almost all children will ignore methods of education or explanation which are beyond the usual comprehensive ability of their age group. The natural reserve of the child who is developing must also be considered, and tactless attempts to intrude into the budding sex life of such persons may lead to a determined opposition and even to gross misunderstanding between the parent or guardian and the child. All such education must be carried out with tact, and should be continued only in so far as the child shows a desire to receive it.

Lastly, sex ethics cannot be separated from ethics in general. An attempt to give mere technical information can be of little value and may be of much harm. The life of instinct and feeling is inextricably bound up with problems of one's attitude toward life and its values. The careful study of this article is warmly advised for all persons who are placed in a position of giving sex instruction to children.

REICHLE, Cleveland.

IMPORTANT REQUIREMENTS IN MODERN HYGIENE. A. GUTWIRTH, Časop. lék. česk. **69**:680 (May 2) 1930.

Because many school children have poor hygienic conditions at home, every effort should be made to have the environment at school as ideal as possible. The author discusses the matter of requirement of air per child, the various window panes that admit ultraviolet rays, school heating, school cleaning, cleaning of blackboards without raising dust, school locations, playgrounds and play apparatus. He stresses the frequent washing of panes, admitting ultraviolet light, because the studies of several workers have revealed marked decrease, as high as 50 per cent, in transmission of light through unwashed panes. Various sanitary codes and regulations for schools are reviewed.

STULIK, Chicago.

DENTITION AS A SIGN OF DEVELOPMENT IN CHILDREN. F. SKALOUD, Zubni lek. (supp., Časop. lék. česk.) **30**:317 (Sept.) 1930.

The author checked the dentition in 894 school boys from 5 to 18 years of age. There was no gross deviation depending on poverty, race, oral hygiene and early infectious disease. The author feels that the dentition may be of use in arriving at the chronological age in medicolegal cases. In checking with a series published by Lukas, dentition in girls begins with the central incisors two months earlier than in boys, and ends seven months earlier with the second molars. Dentition in boys extends from six years and eight months to fourteen years and in girls from six years six months to thirteen years and five months. The eruption of the teeth progresses chronologically with the bodily development.

STULIK, Chicago.

THREE YEARS OF INFANT WELFARE IN A TOBACCO FACTORY IN POLAND. JADWIGA JAROSZEWSKA, Opieka nad dzieckiem **14**:251 (July-Aug.) 1931.

In 1924 the Sejm and the government acknowledge the importance of infant welfare in tobacco factories. They passed Article 15, which specified that wherever one hundred women are employed there must be an infant welfare station and that each woman who has a baby must be allowed to leave her work for two hours in order to nurse it. The babies are supervised by a trained nurse and a pediatrician. The welfare quarters are equipped with a recreation hall, drug department, therapeutic department and physical therapy department. Phosphorized cod liver oil and iron are administered if indicated. Wetnurses are employed when possible. In addition there is a school for mothers which they are compelled to attend.

KRUPINSKI, Chicago.

THE IMMUNITY OF BABIES. J. MUNK, Maandschr. v. kindergeneesk. **1**:311 (April) 1932.

The author considers that immunity in babies is principally explained by an inability to react. A baby has a so-called "anergic immunity."

VAN CREVELD, Amsterdam.

TWO CASES OF INTOXICATION WITH PHENOBARBITAL IN YOUNG CHILDREN. J. C. SCHIPPERS, Maandschr. v. kindergeneesk. **1**:372 (May) 1932.

Two cases of intoxication with phenobarbital in young children are reported. A boy of 1½ years, suffering from epilepsy, received 1 Gm. of phenobarbital instead of 10 mg. Two hours later he was unconscious. The pulse and respiration remained normal. After about thirty-six hours he recovered, but remained somnolent for another twenty-four hours. A girl of 3½ years fell into coma ten minutes after having taken 800 mg. of phenobarbital. After about twelve hours severe motor and psychic unrest appeared. After about two hours the symptoms began to disappear.

VAN CREVELD, Amsterdam.

A CASE OF INTOXICATION BY A POLYMER OF ACETALDEHYDE. A. BAKKER, Nederl. tijdschr. v. geneesk. **75**:5000, 1931.

A case of intoxication by a polymer of acetaldehyde in a boy, aged 5 years, is described. The course was favorable. The tablets are easily mistaken for peppermint by small children; in the author's opinion, it therefore seems advisable to give such tablets some color.

VAN CREVELD, Amsterdam, Holland.

# Society Transactions

## CHICAGO PEDIATRIC SOCIETY

*Clinical Meeting, Nov. 15, 1932*

DR. JULIUS H. HESS, M.D., *Presiding*

PRECOCIOUS PUBERTY. DR. I. MCKY CHAMBERLAIN.

This boy is presented as having preadolescent hypergonadism or macrogenitosomia. He was born on June 30, 1926, and is 6 years and 4½ months old. His father is 29, and has pulmonary tuberculosis of five years' duration. There is one other child, 18 months old, who is well. The mother is well. There have been no other pregnancies. There is no history of any other pathologic condition of the endocrine glands in the family. This boy weighed 7 pounds (3,200 Gm.) at birth. His teeth erupted prematurely, which is common in cases of this kind. He walked at 18 months. His feedings were of average character. He had pertussis at 12 months, measles at 2 years and uncomplicated mumps at 5 years.

He was considered normal until shortly after his third birthday. His growth at that time was about normal, but the external genitalia were large. This is about the usual finding, although some of the children have enlargement of the genitalia earlier. Masturbation was noted at 4 years, and there was a growth of pubic hair at 4½ years. His teeth have become progressively decayed from the fourth year on, another characteristic defect in these cases. This type of child is commonly thought to have perfectly normal intelligence through early childhood, and this boy bears out that finding. His body growth is approximately the average for a boy of 10 or 11 years. He weighs 60 pounds (27,200 Gm.) and is 51 inches tall (129.5 cm.). He is mentally alert, expressive and cooperative. The down present on his face is not that of true hypertrichosis. His hearing and vision are normal, and there are no pathologic ocular findings and no paresis of any of the muscles. There is no evidence of intracranial lesion causing signs of increased intracranial pressure or nerve block; the nose, throat and cervical glands are normal. The heart is normal, and the lungs are normal, except for increased hilar density. There are no palpable tumors in the abdomen.

Laboratory study shows that the blood count, protein nitrogen, serum albumin, serum globulin, calcium and phosphorus were normal. The basal metabolism has varied but is considered normal. The Wassermann test is negative; the Mantoux test, positive. All urinary findings and tests for kidney function showed a normal condition.

Psychologic examination gave normal findings for a boy of 6 years. He passed all the tests for a boy of 7 years except one.

Roentgenograms of the skull are negative; those of the wrists and hands showed overosseous development, with beginning union of the epiphyses at the head of the metacarpus that is commonly seen in a boy aged 16. The other points to be stressed in diagnosis are the enlargement of the external genitalia and the somatic overgrowth.

The pineal gland has always been blamed for precocious puberty, but at present the consensus is to exclude it as a causative agent. The hypophysis has been suspected in these cases, but it does not produce such a picture as this. The gonads are secondarily involved. At present the weight of opinion seems to point to the cause being dependent on the pathologic condition in the suprarenal glands. In this case a further effort to rule out disease of the suprarenals and of the kidney is to be made.

Assuming that the suprarenal glands and a surgical, pathologic condition are ruled out, treatment will rest between the feeding of glandular substances and the

giving of massive doses of roentgenotherapy to the suprarenal glands. The latter offers the more hopeful prospect. Roentgenotherapy to the pineal gland itself is sometimes recommended after every other measure fails.

LYMPHANGIECTASIS WITH CHYLORRHEA. DR. THOMAS SALTIEL.

J. S., a colored boy, aged 12, was admitted to the hospital with the complaint of swelling of the upper part of the left thigh and a white discharge from small vesicles. The general examination was negative, except for small glandular enlargements. There were no stigmas of syphilis. The upper portion of the left leg was from 2 to 3 cm. larger than that of the right. Many vesicles varying in size from that of a millet seed to that of a split pea were present over this area, extending into the inguinal region and on the scrotum up to the raphe.

A white fluid similar in all respects to chyle was obtained by pricking one of the vesicles on the thigh. The Wassermann test of the blood and the Kahn reactions, as well as the chylous fluid, were +4. The spinal fluid was normal.

As to the production of this condition, I feel that syphilis is an incidental finding rather than the responsible factor. There are about sixty-two cases of this condition in the literature. It has been considered by some that this lymphangiectasis is due to a faulty anlage or to weakness of the lymph vessels.

SINO-AURICULAR HEART BLOCK IN CHILDHOOD. DR. GUSTAVE F. WEINFELD.

Because the recorded cases of sino-auricular block are rare, especially in children, it was felt that a report of this case would be of value.

L. T., aged 6, was brought to the clinic because his mother noted that he had tachycardia. He had never complained of any rheumatic symptoms, and, as far as could be determined, he had sustained no recent infection.

Physical examination revealed a moderately well nourished child who was in apparent good health. The findings, except those associated with the heart, were essentially negative. There was a grossly discernible rhythmic variation in the pulse rate, which was dependent on his respiratory rhythm, but in addition to this, there were numerous sudden changes in rhythm which were independent of respirations. There was a soft systolic murmur at the apex, which was not transmitted beyond that point. The area of cardiac dulness was not enlarged. A teleoroentgenogram revealed a heart shadow of normal size and shape. Routine urinalyses and blood counts were normal. An electrocardiogram portrayed typical sino-auricular block.

The child was put to bed at complete rest for several weeks. His temperature remained normal, and the irregularity persisted.

In the course of the next year there were no changes. During this time the pulse rate varied between 78 and 140, the block being present at both the higher and the lower pulse rate levels. The systolic murmur gradually disappeared. He gained weight, attended school and led the life of a healthy, normal child.

On June 27, 1932, he was admitted to the hospital for further study. Atropine was administered in slowly increasing doses. The irregularity did not completely disappear until the twenty-third day of medication, when he was receiving $\frac{1}{30}$ grain (0.00216 Gm.) of atropine sulphate subcutaneously four times a day. This also was the first time that ocular pressure was without effect. By the following day the signs of atropinization had disappeared, and the arrhythmia had returned.

The patient has been under our observation for twenty-six months, and at the age of 8 years, the sino-auricular block is still present.

The sino-auricular block persisted in this patient until he received a total daily dose of $\frac{4}{30}$ grain (0.00864 Gm.) of atropine sulphate subcutaneously. It was at this time only that the oculocardiac reflex could not be obtained. The relationship of the disappearance of the block to atropine, the associated marked sinus arrhythmia and the absence of any other etiologic factors indicate that an abnormal exaggeration of the physiologic activity of the vagus is the immediate and probably solitary cause of the irregularity. This conclusion is in accordance with the views

of Resnick, who believes that "sino-auricular standstill" results from vagal influences on impulse formation in the sino-auricular node, as does also sinus arrhythmia. He says that "sino-auricular standstill is merely a special form of sinus arrhythmia." The association of the two conditions in this patient and the apparent benignity of the process, in spite of its chronicity, are, at least in this instance, a confirmation of Resnick's point of view.

The literature on this type of cardiac irregularity in childhood was reviewed.

The apparent relation of this condition to sinus arrhythmia suggests that it should occur with greater frequency in children.

SUPRASELLAR CYST. (PATHOLOGIC SPECIMEN). DR. ERIC OLDBERG.

The pathologic specimen was the brain of a girl aged 6 who was apparently normal at birth, and who developed normally subsequently. Intellectually she was a little above her age.

When she was 3, she began to have occasional headaches, sometimes associated with vomiting. At first they occurred only once a month, but they increased in frequency and severity until, at the time of admission, they occurred every day. About one and one half years before admission, a progressive loss of vision had begun, until vision had been abolished in the left eye, and there was but a small, upper nasal island of vision in the right eye. For some months before admission the patient had had transitory attacks of diabetes insipidus.

Neurologic examination showed only bilateral advanced primary optic atrophy; roentgenograms of the skull showed faint areas of calcification above the sella turcica.

This history and these findings are typical of one of the two commonest intracranial tumors of childhood, the other being glioma of the midline of the cerebellum. The particular tumor from which this child suffered is perhaps best called craniopharyngioma, although it is variously called suprasellar cyst, Rathke's pouch cyst and craniopharyngeal pouch cyst.

Although we operate on these patients and usually alleviate their symptoms for some time, no one has as yet effected a permanent operative cure. The child whose brain I have presented was operated on, but despite the fact that nothing was done except the aspiration of about 2 ounces of chocolate-colored fluid filled with cholesterol crystals, an immediate postoperative hyperthermia developed, and she died. The only explanation of death that I can give is that perhaps the tumor, which was unusually large, collapsed and pulled on important hypothalamic centers.

BLOOD TYPES IN HEMOPHILIA. DR. CARROLL LAFLEUR BIRCH.

In 1926, Dr. Kubanyi published an article on blood types in hemophilia in the *Klinische Wochenschrift* (**5**:321 [Feb. 19]). He observed that in hemophiliac families the males whose group corresponded to that of the mother were afflicted with hemophilia, while those of different groups escaped. He further observed that group IV appeared to be the most prevalent type in patients with severe hemophilia.

With this in mind my associates and I typed the blood of some of the members of ten of our hemophiliac families. This was done by the method of Moss, types II and III serums being used. No specific agglutinins were employed.

The results are summarized in the following statements:

1. Of the sixteen transmitters, one was in group I, four in group II, six in group III and five in group IV.

2. Of the seventeen hemophiliac patients, there were none in group I, six in group II, four in group III and seven in group IV.

3. Of the fifteen instances in which the blood of the mother and of the hemophiliac son was typed, the blood of nine sons was of the same type as the mother's, and that of five was different. In one instance the blood of the mother, father and son was of the same group. The blood of two normal sons was of the same type as the mother's.

4. There were three instances in which the blood of three generations was available for typing, that of the patient with hemophilia, his mother's and his maternal grandmother's. In one of these the blood of all three was of the same type. In one the grandmother's and mother's blood were of the same type, while that of the patient with hemophilia was different; in the third the blood of the mother and of the son was of the same type, while that of the grandmother was different.

We concluded from this brief and rather superficial study that at least in our group there was not sufficient consistency in the blood types to be of any significance.

STUDIES IN CRETINISM AND HYPOTHYROIDISM IN CHILDHOOD: I. BLOOD CHOLESTEROL. DR. I. P. BRONSTEIN.

This study on the basis of blood cholesterol has as its objective, first, the establishment of an additional method for regulating thyroid therapy and, second, an improved understanding of the clinical course of the child deficient in thyroid. As one follows these children from month to month, the impression is gained that the basal metabolic rate as ordinarily determined by present clinical methods in young children is unreliable. The basal metabolic rate, although valuable, is not a specific test, and as DuBois indicated in cretinism, the comparison with normal standards often presents great difficulties. The basal metabolic rate, therefore, should not be the principal guide in the progress of these patients. Furthermore, clinical impressions have many limitations.

Mindful that the exact mechanism regulating cholesterol metabolism is obscure, this investigation was undertaken for the purpose of determining the relationship of blood cholesterol in children deficient in thyroid, with the possibility of its use as a corroborating test in controlling the dosage of thyroid and maintaining metabolism at a normal level.

In order to establish an average blood cholesterol for the group, the values of this lipid were determined in twenty hospitalized and five ambulatory children. The determination excluded nephrosis, nephritis, diabetes mellitus, purpuras, anemias and blood dyscrasias, as well as other conditions in which cholesterol metabolism may be definitely altered. The average level of blood cholesterol in this group was 190+.

Hypercholesteremia existed in the children. Of the series under consideration, eight of the patients were male, ranging in age from 4 months to 16 years, the only female member of the group being 13 years old. The average cholesterol value in the children not receiving thyroid was 428 mg. per hundred cubic centimeters, the lowest value being 277 mg. in the youngest, and the highest, 782 mg. in the female cretin. The average cholesterol value for the group under treatment was 171 mg., the only determination above 200 mg. being in one boy whose carpal bones showed at onset of treatment ossification approximately equivalent to that of a 1 year old child. We were unable to obtain in this patient a basal metabolic rate sufficiently accurate and satisfactory. He had received ¾ grain (0.0486 Gm.) of thyroid a day prior to admittance, at which time the cholesterol value was 227 mg. After several weeks without thyroid, the cholesterol value rose to 313 mg., and on receiving therapy, the cholesterol fell 96 points.

When it is impossible to obtain basal metabolic rates in older children, owing to unmanageability, or in infants because of lack of enclosed respiratory chambers, cholesterol determinations may aid.

It should be borne in mind that the majority of these children were under treatment before the study began, and as it is impossible to withhold thyroid from these children for too long periods without serious parental objections, the cholesterol determinations may not represent the maximum high values. However, merely eliminating thyroid for short periods in a previously treated child with low cholesterol brings not only a return of hypothyroid characteristics but a definite rise of cholesterol.

Although it is not safe to speculate here as to the cause of the excess of this so-called lipid, a relationship between cholesterol, the basal metabolic rate and the dosage of thyroid exists. The feeding of thyroid definitely lowers the cholesterol, raises the basal metabolic rate and effects clinical improvement.

My associates and I were interested in the possibility of influencing cretins by other means, as, for example, with insulin, as suggested by Chamberlain, since insulin will diminish the hypercholesteremia in diabetes. The pancreatic hormone was used for forty-three days, during which period medication with thyroid was stopped. The cholesterol rose from 200 to 454 mg., and the basal metabolic rate fell from 0 to —35. When treatment with thyroid was again instituted, the cholesterol fell to 208 mg., a fall of 246 points, and the basal metabolic rate gradually rose 71 points. In the course of a little over two weeks, the thyroid was rapidly increased from 1 to 8 grains (0.065 to 0.52 Gm.), and the patient was kept on this large dose for a short period, following which a complete change in his appearance and mental reaction took place.

The use of cholesterol as an aid in the diagnosis and regulation of thyroid dosage offers definite possibilities.

### Osteitis Fibrosa Cystica. Dr. H. G. Poncher.

There are a number of bone dystrophies of unknown origin which, though presenting a varying clinical course, show in common the fundamental histologic picture of osteitis fibrosa. This group of diseases has been considered a disease of adult life. It becomes increasingly apparent with the more intensive study of the pathogenesis of the osteitis fibrosa group that not a few cases have their inception in childhood. They are recognized in adult life after the pathologic condition is well established, and present obvious clinical signs. Two cases of this group which brought out these points are presented.

Robert and Elsie are 12 years of age. The only presenting symptom was repeated spontaneous fractures of the lower extremities. This was noted at the ages of 5 and 6 years, respectively. Until their admission to this hospital they had been under the care of an orthopedist. The boy presented clinical and roentgenographic features of osteitis deformans (Paget's disease) with leontiasis ossea, together with the features of osteitis fibrosa cystica (Recklinghausen's disease). The girl shows findings more characteristic of osteitis fibrosa cystica.

Blood calcium and phosphorus are normal in both cases. A careful study of the metabolism of these salts reveals, however, that they are in negative phosphorus and calcium balance.

Since 1926, when Mandl of Vienna removed an adenoma of the parathyroid in a typical case of osteitis fibrosa cystica, the conception of this group of diseases as a clinical expression of hyperparathyroidism has been extant. Time does not permit a historical or comprehensive discussion of this subject, but there are numerous articles on this relationship that bring out many points involved in this discussion. Clinically, there has been much confusion in diagnosis rising from a desire to create entities not warranted by pathologic and metabolic facts. For example, leontiasis ossea is probably nothing more than a hyperostotic involvement of the skull in osteitis fibrosa.

It is unfortunate for this presentation that the children have not had their parathyroid glands explored, but there is every reason to believe that they are orthodox members of the osteitis fibrosa group. I am of the opinion that in the future, with the improved methods of diagnosis and a more comprehensive understanding of this disease, more cases will be described in children.

### Enterogenous Cysts and Diverticula. Dr. G. Milles.

The group of cysts and diverticula of enterogenous origin which because of their position and relation to the intestine can be separated from the classic Meckel's type is illustrated by the following case.

A white boy aged 18 months was seized with violent cramplike abdominal pain. The attacks recurred at irregular intervals, sometimes associated with the passage of bright red blood. During the third year the hemorrhages had caused marked anemia and weakness. A roentgenogram of the chest revealed a large globular mass in the right side, displacing the heart to the left, with a defect of the vertebral bodies from the fourth to the seventh vertebrae. The mass was resistant to roentgen therapy, and the patient died following its removal.

The necropsy findings were a second cystic mass in the mediastinum not found at operation, filled with thin, serous fluid containing many cholesterol crystals, and a diverticulum lying between the leaves of the mesentery and arising 20 cm. above the ileocecal valve, communicating with the small intestines at this point and by a second opening about 10 cm. above the first. There was a superficial ulceration at the margin of the first communication. The diverticulum simulated grossly the small intestine, except in its distal 8 cm., where a polypoid mass was present, and beyond this, two incompletely separated cysts. It measured 51 cm. in length and lay in close approximation to the small bowel thoughout its course, except at the distal 8 cm., where a small segment of mesentery intervened.

Microscopically, the cysts of the chest were found to be made up of gastric tissue, the mucosa being preserved in one area and simulating the pyloric tissue. The wall of the diverticulum corresponded to small intestinal mucosa in its microscopic picture, and the polypoid mass near the terminus corresponded to gastric mucosa.

The epithelial nodes of Lewis and Thyng found in embryos from 5 to 42 cm. by several authors would best explain the embryologic origin of the anomalies described.

# Book Reviews

**Poliomyelitis.** International Committee for the Study of Infantile Paralysis. Price, $6. Pp. 562, with 31 illustrations, 19 charts and 82 tables. Baltimore: Williams & Wilkins Company, 1932.

Mr. Milbank, who was always interested in the progress of medicine, but was made especially conscious of what scientific research could do by an experience in his own family, organized the International Committee for the Study of Infantile Paralysis, and provided funds for its work. It is headed by William H. Park, chairman, and Josephine B. Neal, secretary, and is composed of the heads of a number of laboratories here and abroad. Forty-two workers have been financed, and the results of their work are published in various journals. This study is but indirectly concerned with their work. It deals instead with the whole literature of poliomyelitis, which now includes about 8,000 references. The more important of these are appended in the bibliography at the end of the book. This work was done by Dr. Helen Harrington, assisted by Dr. Mildred W. Wells and Miss Elizabeth F. Hutchins, aided and directed by Dr. Josephine B. Neal, who wrote the chapters on symptomatology and treatment. The articles on etiology, resistance and immunity and pathology are by Dr. Harrington, and that on epidemiology is by Dr. Wells; there is a short historical summary by Miss Hutchins.

Any one who has seen Dr. Neal's review of the literature of encephalitis will know at once what a valuable book this one on poliomyelitis is; but it is far wider in scope and far more comprehensive in the handling.

There are 31 illustrations and 82 tables scattered through the 478 pages of text, while the bibliography covers 43 pages.

It is difficult in a short review to present adequately the material set forth. The historical review had to be condensed, but it takes in the ancient records and divides the more modern times into the periods of clinical observation, pathologic investigation, epidemiologic interpretation and experimental contribution, bringing the disease down to the present time.

The chapter on etiology considers in sufficient detail the virus and its properties, its distribution in the body and experimental disease. Of great interest, too, is the chapter on resistance and immunity, in which the neutralizing substances, active immunization and immune serums are fully covered as far as knowledge goes at present.

The symptomatology is considered as regards the various manifestations of the disease, and the different classifications are given, but Neal divides the cases into the abortive, nonparalytic type with subcortical paralysis, the cerebral or encephalitic type and the atoxic type. It would not seem out of place to suggest a meningitic type as a subheading, to call attention to some cases in which the diagnosis is often wrong when the physician has not had a large experience with the disease, and but few have. The treatment as it is now understood is adequately outlined for the acute cases, but it seems a pity that for a book which will have a wide circulation some account of the after-treatment and the details of physical therapy in its application to poliomyelitis were not included. It would have been a great help in informing the medical profession what may be done for many patients, many of whom are only too often neglected.

The chapter on pathology covers the subject fully, and the one on epidemiology is a scholarly presentation of unusual interest. The newer ideas, which are too little considered in America, are gone into. These include the possibilities of water, milk and insects. The question of transmission is not settled, and it is highly probable that the disease may be spread in a number of ways. Heretofore epidemiologists have been trying largely to find a single means of transmission.

Mr. Milbank, the committee and the authors are to be congratulated on producing a book that is by far the most satisfactory work to date with which the

reviewer is familiar, a masterpiece in reviewing and presenting succinctly a mass of literature made inaccessible by the time factor, if not by its location. It is heartily commended.

**Children's Tonsils In or Out.** By Albert D. Kaiser, M.D. Price, $5. Pp. 293, with 1 illustration. Philadelphia: J. B. Lippincott Company, 1932.

The conclusions of the author of this book are based on ten years of careful study, during which a group of 2,200 school children who had had their tonsils and adenoids removed are compared as to susceptibility to disease with 2,200 children in similar surroundings who, although presenting the indications for an operation on the tonsils and adenoids, had failed to have it done.

The opening chapters contain a brief historical sketch of the operation, the anatomy and possible function of the tonsils and the bacteriologic and pathologic findings in these organs.

The statistical report concerns the results of careful study of these two groups of children as to their susceptibility to sore throat, head colds, otitis media, laryngitis, bronchitis and pneumonia, kidney infections and the communicable diseases of childhood.

The children whose tonsils and adenoids had been removed presented fewer cases of sore throat, head colds, otitis media, heart disease and rheumatic fever. They showed a greater susceptibility to laryngitis, bronchitis and pneumonia, while such diseases as asthma and hay fever were equally prevalent in both groups.

The concluding chapters contain an able discussion of the indications and contraindications for tonsil and adenoid operation in children and of the hazards encountered during the operation. The author is not favorably impressed with electrosurgery in the removal of tonsils of children because of the inability to get the patient's full cooperation.

No one on whom the decision as to the advisability of the removal of tonsils and adenoids of children rests should fail to read this able treatise by an impartial observer.

**Diseases of the Spinal Cord.** By Williams B. Cadwalader, M.D. Price, $5. Pp. 196, with 72 illustrations. Baltimore: Williams & Wilkins Company, 1932.

Dr. Cadwalader offers in short compass a manual covering the more common diseases of the spinal cord which in many respects is superior to most of the texts of larger scope published in English. Its chief attractions lie in the attempt at a rational presentation of the cord syndromes encountered as opposed to a meaningless recitation of isolated symptoms and in its modernity. The influence of a large and well selected bibliography is evident throughout the work.

On the whole, the sections dealing with individual diseases are superior to those on the anatomy, physiology and pathophysiology of the spinal cord. In the latter, brevity is too often achieved at the cost of inadequacy or ambiguity. For example, the section on the innervation of the urinary bladder lacks clearness and completeness, a serious defect in a work of this kind. The presentation of the sensory pathways of the spinal cord, which includes a good summary of Foerster's conceptions of the topography of the anterolateral tracts, is an instance of the author's success in writing a textbook that is contemporary. However, at times this tendency has led to the inclusion of material too controversial for an elementary textbook, such as the position that spasticity from lateral column degeneration is essentially a result of disturbed conduction in the rubrospinal tract, and the doctrine of antidromic sensory fibers in the anterior roots.

The chapter on progressive muscular dystrophy is especially commendable. The inclusion of the views of Ken Kuré on the relationship of this condition to disturbances of the sympathetic nervous system is most timely. Although the pathologic sections are superficial in places and the chapter on syphilis is entirely too brief, the clinical portion of the book is admirably executed.

**Cultivating the Child's Appetite.** By Charles Anderson Aldrich, M.D. Second edition. Price, $1.25. Pp. 137. New York: The Macmillan Company, 1932.

Knowledge of dietetics has made noteworthy advances in the past decade, and people in general have become well informed on the foods included in the so-called proper diet. However, insistence on the child eating prescribed kinds and amounts of food has led frequently to objection from the child, manifested by poor appetite, refusal of food and behavior problems. Dr. Aldrich discusses this situation from the standpoint of a pediatrician who has had years of experience and has devoted considerable study to the problem.

The technic of feeding and the psychologic considerations involved are stressed chiefly. The factors affecting a child's appetite are thoroughly presented, as well as practical suggestions on the prevention and cure of anorexia. This book should be of great value not only to mothers, by whom it can be easily read and understood, but also to nurses, physicians and psychologists who deal with children.

The second edition of this book contains an additional chapter in which the developments of the past five years are discussed in their relation to the appetite. Such developments include vitamin B, the daily amount of milk, body type, gastro-intestinal physiology and secretions of the endocrine glands.

**Précis clinique et opératoire de chirurgie infantile.** By L. Ombrédanne. Price, 140 francs. Pp. 1,462. Paris: Masson & Cie, 1932.

This book is just what the name would indicate. It is well illustrated both with actual photographs and with diagrams, and it is well fitted to meet the needs of one who wishes to find out something about the surgical conditions at this age. The author has paid especial attention to many of the rare conditions, surgical operations for which are detailed, many of them being operations with the author's own technic. Not only is operative technic given, but much in the way of orthopedic maneuvers and other treatments. For a book of this size and for a subject so comprehensive, the work is well done.

# Directory of Pediatric Societies

## INTERNATIONAL

### International Association of Preventive Pediatrics

President: Professor Taillens, Lausanne, Switzerland.
Secretary: Dr. P. Oltramare, rue Decandolle, Geneva, Switzerland.

### International Pediatric Congress

President: Dr. George Frederic Still, 28 Queen Anne St., London, W. 1.
Secretary: Dr. Leonard K. Findlay, 61 Harley St., London, W. 1.
Place: London. Time: July 20-23, 1933.

## FOREIGN

### Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. Leonard G. Parsons, 58, Calthorpe Road, Birmingham, England.
Secretary: Dr. W. G. Wyllie, 33, Wimpole St., W. 1, London.
Place: London. Time: May 26, 1933.

## NATIONAL

### American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Frederic W. Schlutz, Bobs Roberts Hospital, University of Chicago, Chicago.
Secretary: Dr. Alfred A. Walker, Highland Plaza Apartments, Birmingham, Ala.
Place: Milwaukee. Time: June 12-16, 1933.

### American Academy of Pediatrics

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.

### American Child Health Association

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. Philip Van Ingen, 125 E. 71st St., New York.

### American Hospital Association, Section on Children's Hospitals

President: Dr. Thomas B. Cooley, 7815 E. Jefferson Ave., Detroit.
Secretary: Miss Bena M. Henderson, 721 N. 17th St., Milwaukee.

### American Pediatric Society

President: Dr. Oscar M. Schloss, 1185 Park Ave., New York.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid, St. Louis.
Place: Washington, D. C. Time: May 8-10, 1933.

### Association of American Teachers of the Diseases of Children

President: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Secretary: Dr. Oscar Reiss, 1930 Wilshire Blvd., Los Angeles.

### Canadian Society for the Study of Diseases of Children

President: Dr. Frederick F. Tisdall, 170 St. George St., Toronto, Ontario.
Secretary-Treasurer: Dr. T. G. H. Drake, 67 College St., Toronto, Ontario.

### Society of Pediatric Research

President: Dr. Bengt Hamilton, University of Chicago, Chicago.
Secretary-Treasurer: Dr. Charles F. McKhann, Harvard Medical School, Boston.
Place: New York. Time: May 6, 1933.

## SECTIONAL

### Central States Pediatric Society

President: Dr. Frank C. Neff, 406 W. 34th St., Kansas City, Mo.
Secretary: Dr. A. H. Parmelee, 715 Lake St., Oak Park, Ill.

### North Pacific Pediatric Society

President: Dr. Herbert E. Coe, 509 Olive St., Seattle.
Secretary: Dr. Raymond H. Somers, Cobb Bldg., Seattle.
Place: Seattle. Time: Jan. 28, 1933.

### Southern Medical Association, Section on Pediatrics

Chairman: Dr. Horton Casparis, Vanderbilt University Hospital, Nashville, Tenn.
Secretary: Dr. Luther W. Holloway, 117 W. Duval St., Jacksonville, Fla.

## STATE

### Alabama Pediatric Society

President: Dr. Thomas J. McElhenney, 1722, 2nd Ave., Bessemer.
Secretary-Treasurer: Dr. John W. Simpson, 1117 S. 22d St., Birmingham.

### Georgia Pediatric Society

President: Dr. M. Hines Roberts, Atlanta.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.

### Louisiana State Pediatric Society

President: Dr. Cecil O. Lorio, 245, 3d St., Baton Rouge.
Secretary-Treasurer: Dr. Maud Loeber, 3503 Prytania St., New Orleans.

### Medical Society of State of New York

Chairman: Dr. Brewster Doust, 605 Medical Arts Bldg., Syracuse.
Secretary: Dr. G. C. Sincerbeaux, 6 William St., Auburn.

### Nebraska Pediatric Society

President: Dr. W. O. Colburn, 724 Sharp Bldg., Lincoln.
Secretary-Treasurer: Dr. C. G. Weigand, 1614 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Second Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

### North Carolina Pediatric Society

President: Dr. Yates W. Faison, 121 W. 7th St., Charlotte.
Secretary: Dr. E. K. McLean, 121 W. 7th St., Charlotte.
Place: Various children's hospitals. Time: Twice a year.

### Oklahoma State Pediatric Society

President: Dr. Clark H. Hall, 117 N. Broadway, Oklahoma City.
Secretary: Dr. M. J. Searle, 108 W. 6th St., Tulsa.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. T. D. Dotterer, 1512 Marion, Columbia.
Secretary-Treasurer: Dr. Julian P. Price, 117 W. Cheves St., Florence.

TEXAS PEDIATRIC SOCIETY

President: Dr. Boyd Reading, 2201 Avenue D, Galveston.
Secretary-Treasurer: Dr. F. W. Hoehn, 1006 Medical Arts Bldg., Waco.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. St. Geo. Grinnan, 925 W. Grace St., Richmond.
Secretary-Treasurer: Dr. J. B. Stone, 2042 Park Ave., Richmond.

WEST VIRGINIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

President: Dr. George M. Lyon, 955, 4th Ave., Huntington.
Secretary: Dr. M. F. Petersen, 1013 Quarrier St., Charleston.

## LOCAL

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

Chairman: Dr. J. E. McClelland, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. P. G. Albrecht, 2009 Adelbert Rd., Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

Secretary: Dr. Lawrence Murray, 1870 Bloor St., W., Toronto.
President: Dr. Gladys Boyd, 56 DeLisle St., Toronto.

BRONX PEDIATRIC SOCIETY

President: Dr. Henry M. Eisenoff, 1018 E. 163rd St., New York.
Secretary: Dr. Morris Gleich, 9 Post Ave., New York.
Place: Concourse Plaza, 161st St. and Grand Concourse. Time: Second Wednesday of each month, except June, July, August and September.

BROOKLYN PEDIATRIC SOCIETY

President: Dr. Irwin Schiff, 658 Eastern Parkway, Brooklyn.
Secretary: Dr. Louis A. Koch, 62 Pierrepont St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Fourth Thursday of October, January and April.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Archibald L. Hoyne, 25 E. Washington St., Chicago.
Secretary: Dr. Bert I. Beverly, 8 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

DALLAS COUNTY PEDIATRIC SOCIETY

President: Dr. Gordon B. McFarland, Medical Arts Bldg., Dallas, Texas.
Secretary: Dr. Harold T. Nesbit, Medical Arts Bldg., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

### Detroit Pediatric Society

President: Dr. Bernard Bernbaum, 5057 Woodward Ave., Detroit.
Secretary: Dr. Sarah S. Schooten, 5057 Woodward Ave., Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

### Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Secretary: Dr. T. I. Willingham, 384 Peachtree St., Atlanta.
Place: Academy of Medicine, 32 Howard St. Time: Second Thursday of each month from October to April, 8 p. m.

### Memphis Pediatric Society

President: Dr. William R. Graves, 1193 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry J. Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

### Milwaukee Pediatric Society

President: Dr. G. H. Fellman, 231 W. Wisconsin Ave., Milwaukee.
Secretary: Dr. George F. Kelly, 161 W. Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

### New England Pediatric Society

President: Dr. Lewis Webb Hill, 319 Longwood Ave., Boston.
Secretary: Dr. Gerald Hoeffel, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

### New York Academy of Medicine, Section of Pediatrics

Chairman: Dr John Caffey, 50 Haven Ave., New York.
Secretary: Dr. Harry Bakwin, 132 E. 71st St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

### Northern California Pediatric Society

President: Dr. Edward B. Shaw, 384 Post St., San Francisco.
Secretary-Treasurer: Dr. Lloyd Hardgrave, 384 Post St., San Francisco.
Place: Various teaching schools. Time: Monthly.

### Northwestern Pediatric Society

President: Dr. Irving McQuarrie, Dept. Pediatrics, University of Minnesota, Minneapolis.
Secretary: Dr. Alexander Stewart, 459 Lowry Medical Arts Bldg., St. Paul.

### Philadelphia Pediatric Society

President: Dr. John P. Scott, 2040 Pine St., Philadelphia.
Secretary: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala-Cynwyd, Pa.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

### Pittsburgh Pediatric Society

President: Dr. Henry C. Flood, 119 S. Highland Ave., Pittsburgh.
Secretary: Dr. E. R. McCluskey, Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

### Richmond Pediatric Society

President: Dr. John S. Weitzel, 3103 W. Franklin St., Richmond, Va.
Secretary-Treasurer: Dr. W. E. Chapin, 922 Floyd Ave., Richmond, Va.
Place: Retreat for the Sick, 2621 Grove Ave. Time: First Thursday of each month (other than during the summer).

### Rochester Pediatric Society

President: Dr. S. W. Clausen, Strong Memorial Hospital, Rochester, N. Y.
Secretary: Dr. F. W. Bush, 29 N. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month from October to May.

### Rocky Mountain Pediatric Society

President: Dr. C. H. Platz, Fort Collins, Colo.
Secretary: Dr. R. H. Verploeg, 1850 Gilpin St., Denver.
Place: Children's Hospital, Denver. Time: Third Saturday of each month from September to May, inclusive, 2:30 p. m.

### St. Louis Pediatric Society

President: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, Beaumont Bldg., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

### Seattle Pediatric Society

President: Dr. C. L. Smith, 1215, 4th Ave., Seattle.
Secretary: Dr. N. W. Murphy, 515 Cobb Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 7 p. m.

### Southwestern Pediatric Society

President: Dr. Donald K. Woods, 2545 4th Ave., San Diego, Calif.
Secretary: Dr. Jeanette Harrison, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January. March, May, September and November.

### University of Michigan Pediatric and Infectious Disease Society

President: Dr. Henry G. Poncher, 5325 Kenmore Ave., Chicago.
Secretary: Dr. John P. Parsons, 320 S. Division St., Ann Arbor, Mich.